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Original Articles

FACTORS INVOLVED IN DRUG-PRODUCED MODEL PSYCHOSES*

By

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(1) The Problem and Its Experimental Approach

The use of fibrous wool protein as a model of the structural surface of receptors, possibly involved in the mechanism producing a model psychosis by drugs, was suggested by three lines of evidence.

First, the strong affinity (sorption) of certain basic compounds to keratins of low sulphur content as exemplified by the Gram-positiveness of epidermal (Fischer, 1953c) and nervous (Bailey, 1950) tissue.

Second, the accumulating evidence indicating the similarity in behaviour between keratins of high sulphur content (e.g. wool) and the protein component of certain cell membranes (Fischer, 1951; Fischer and Larose, 1952a; *idem*, 1952b; Larose and Fischer, 1952; *idem*, 1953a and 1953b).

Third, some preliminary experiments confirming the role of wool protein as a useful model to simulate some of those receptors for which certain drugs appear to compete.

(1) It was well known that methylene blue, which competes with acetylcholine in causing contraction of an isolated frog heart (Clark, 1937) can be seen by its blue colour absorbed to the tissue from which even prolonged washing does not dislodge it. This example of a competitive absorption (displacement) could be simulated in a model experiment showing the high affinity of methylene blue chloride ‡ to wool, i.e. $3 \cdot 3 \times 10^{-2}$ millimoles per 1 gm. of wool, whereas acetylcholine bromide§ could be washed out completely (desorbed) from the wool under the same experimental conditions.||

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‡ National Aniline Div. product; C.I. No. 922.

§ An Eastman Organic chemical.

|| A slight modification of the procedure previously described (Fischer, Hoelle and Seidenberg, 1951) was introduced this time: after equilibrium has been reached, each of the wool samples was rinsed three times by immersion in individual beakers, containing 250 cc. of distilled water at 29-30° C., each rinsing requiring a fresh water change.

(2) The adrenergic blocking action of compounds of the Dibenamine (β-haloalkylamine) type (e.g. SKF-501=N-(9-fluorenyl)-N-ethyl-β-chlorethylamine hydrochloride) was felt to be another example of an inhibition of the action of epinephrine (adrenaline) by means of competitive absorption on a receptor (target) presumably proteinic in nature. Such a hypothesis is supported by some indirect evidence; Sawyer and Parkerson, 1953, namely were able to demonstrate the ability of SKF-501 to block the effects of epinephrine on its target organs, Schayer *et al.*, 1953, on the other hand observed a significant increase in the rate of destruction of l-epinephrine after Dibenamine administration. In line with the foregoing conclusions and results we measured a higher affinity (absorption) of SKF-501 for wool, i.e. $3{\cdot}8\times10^{-2}$ millimoles per gm. wool, than that of epinephrine. In order to prevent oxidation of the latter, the determination of its affinity for wool had to be carried out in the presence of very small amounts of ascorbic acid but even so we may make only an estimated comparison.

Based on these premises, the affinity for wool* (Fischer, Hoelle and Seidenberg, 1951) of the following four basic compounds was determined at pH 5·2: mescaline hydrochloride, methedrine hydrochloride, lysergic acid monoethylamide (LAE) and lysergic acid diethylamide (LSD) the latter two in form of their methanoltartrates. These drugs if administered to humans in the approximate range of dosage: 500 mg., 100 mg., 1 mg. and 100γ respectively, cause a model psychosis characterized by hallucinations and related phenomena of similar intensity and duration (Behringer, 1927; Mayer-Gross *et al.*, 1951, 1953; Stoll, 1947; Liddell and Weil-Malherbe, 1953; Solms, 1953; Fischer, 1946; Fischer, Georgi and Weber, 1951). The method of determining the affinity for wool used in this study gives only relative values but these were found to be proportional to the absolute values obtained by another method (Larose and Fischer, 1953b).

(2) Results

The results are presented in Fig. 1. The logarithms of dosage of each of the four compounds which causes a model psychosis of comparable intensity and duration are plotted against the amount of these compounds sorbed by wool. The results indicate that the higher the affinity of a drug for wool, the lower the amount of that drug required to cause hallucinations.

The results are not contrary to the hypothesis that the mode of action of mescaline and LSD might be different (Witt, 1951; Mayer-Gross *et al.*, 1953). Block and Block, 1952; Block, 1953, have shown that C^{14} mescaline is incorporated enzymatically and not by absorption on the liver protein at the peak of hallucinatory phenomena. The yield and speed of this reaction was found to be in the same range of magnitude as that of radioactive labelled lysine (Block and Block, 1952). Our results are in line with this evidence since they show no affinity of DL-lysine hydrochloride and mescaline hydrochloride for wool. Another analogy: β-phenylethylamine, a sympathomimetic compound which in contradistinction to mescaline, benzedrine, ephedrine, etc., is regarded as a normal metabolite was shown to be degraded enzymatically to phenylacetic acid (Block, 1953). Thus, mescaline has neither its mescalinoxidase nor an affinity to (liver) protein; β-phenylethylamine, however, has its amino oxidase and therefore may be absorbed on (liver) protein. In accordance with this we found that β-phenylethylamine has an affinity of $2{\cdot}2\times10^{-2}$ millimoles for 1 gm. (wool) protein.

* The term wool is identical with that of intact wool used in some previous papers, see e.g., Fischer and Larose, 1952b.

	Affinity i.e. average millimoles $\times 10^{-2}$ of drug sorbed by 1 gm. of wool	Single dose of drug	log. of single dose
Mescaline	0	0·5 gm.	−0·3
Methedrine	0·6	0·1 gm.	−1·0
LAE	1·1	1 mg.	−3·0
LSD	2·6	100γ	−4·0

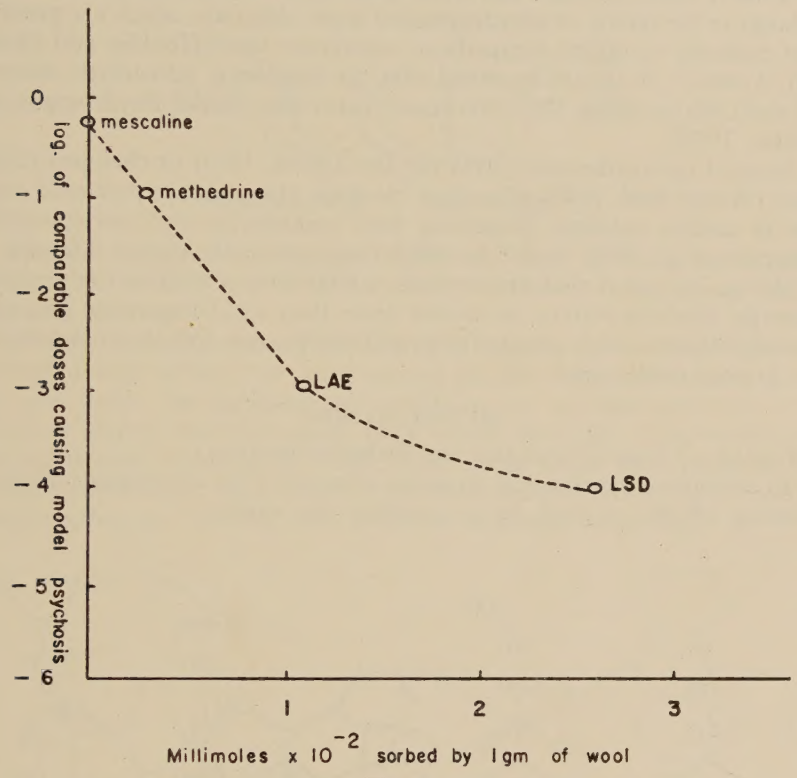


Fig. 1.

(3) Discussion

We are inclined to attribute the increasing affinity of the drugs in question for wool* to their different degrees of specificity simulating a reversible inhibition of an equilibrium involved in the production of hallucinations.

We included only these four drugs in Table and Fig. 1, because it is not easy to find other drugs which precipitate a reversible model psychosis with hallucinatory experience of comparable duration and intensity after administration of a *single* dose. Atabrine (mepacrine), e.g. which is known to produce hallucinations and catatonic excitement (Greiber, 1947; Szatmari, 1953), requires prolonged daily administration.† Another antimalarial, of similar structure and action, Pentaquine, displays an affinity of $3{\cdot}6 \times 10^{-2}$ millimoles per 1 gm. of wool. If Pentaquine is administered daily at a dosage four times higher than usual

* High affinity for wool does not mean the same for us as "selective absorption". An example: Bradley (1951) has shown the selective absorption of one of the optical antipodes by wool from an aqueous or alcoholic solution containing both of the optical antipodes of resolvable acids.

† E.g. 3 gms. per day for 8 days (Halpern, *et al.*, 1953); accordingly we find the affinity for wool of atabrine to be low, i.e. $0{\cdot}9 \times 10^{-2}$ millimoles/gm. This example suggests that compounds of low affinity for wool seem to display their biological activity only in high dosage.

(0·12-0·24 g./day), it acts as an adrenergic blocking agent (Hoobler and Dontas, 1953). This feature seems to be, among others, a common characteristic of drugs capable of precipitating a model psychosis.

Liddell and Weil-Malherbe, 1953, have shown that methedrine as well as LSD also block adrenergic activity by lowering the blood-epinephrine level, after a short initial increase, during the model psychosis; so might LAE, since it belongs to the family of dihydrogenated ergot alkaloids, which are presumed to act centrally to inhibit sympathetic vasomotor tone (Hoobler and Dontas, 1953); however, it should be noted that the peripheral adrenolytic effects of LAE and LSD are about 300-2,000 times weaker than that of dihydroergotamine (Rothlin, 1953).

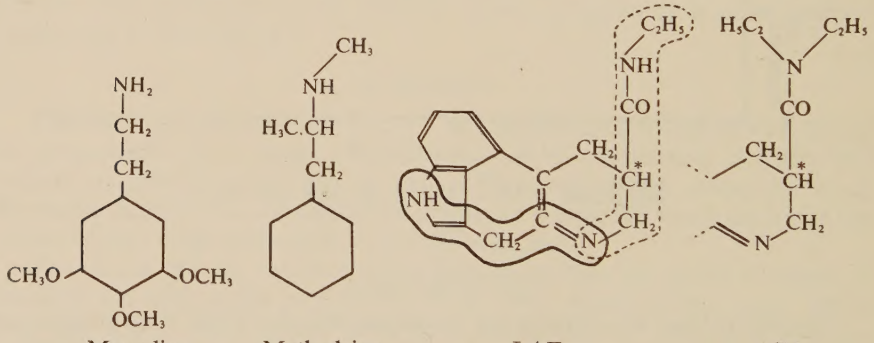
Surgical (sympathectomy) (Harrer and Urban, 1953) or chemical (Dibenamine) (Walter-Buel, 1949) adrenergic blockage also produce psychotic experiences in certain subjects, possessing high epinephrine and nor-epinephrine (Nickerson *et al.*, 1953) levels* to which they apparently are not adapted.

Hence, it appears that drugs which exhibit their central and/or peripheral adrenergic blocking activity in smaller doses than e.g. Dibenamine and simultaneously display a high affinity for (wool) protein, are able to cause hallucinations in very small doses.

(4) Speculations

A. Related to Chemical Structure and Biological Activity

In examining the chemical structure of some of the compounds displaying ncreasing affinity to wool, let us consider one aspect.



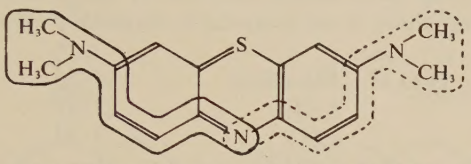
Mescaline Mol. w.: 211·6 | Methedrine Mol. w.: 149·1 | LAE Mol. w.: 295 | LSD Mol. w.: 323

Bovet *et al.*, 1952 and 1953, have shown that the part mainly responsible for specific pharmacodynamic activity of dehydrogenated ergot alkaloids is the molecular configuration centered at the primary NH_2-group and its neighbourhood. We can extend this observation to almost all of our compounds involved in this report and compare in a deliberately oversimplified way the aforementioned groups on these compounds as one factor supposedly influencing their increasing *absorption* (affinity) *for wool.* From mescaline to methedrine: there is an additional monomethyl group on the primary amino N. The third drug, LAE also has an alkylated primary amino group (monoethyl) and then a three C-chain counting up to its additional N in the nucleus of the formula; the latter initiates a second N–C–C–C–N– grouping; LSD, the fourth drug, differs

* Only about 20 per cent. of hypertensive patients react to 0·5 gm. Dibenamine with a model psychosis (Walter-Buel, 1949).

from LAE only by a higher grade of alkylation on the primary amino group (di-ethyl). Hence we note that (1) a gradually higher grade of alkylation and (2) the presence of two "LSD-tails" (N–C–C–C–N) are among the structural concomitants of our basic drugs displaying an increasing selectivity for wool.

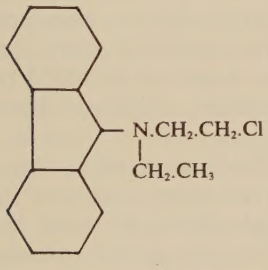
The next formula, methylene blue, shows us a substance of even higher affinity (i.e. absorption) for wool than LSD.



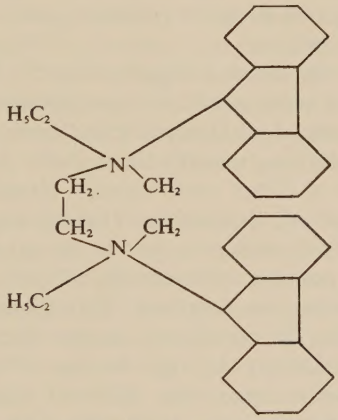
Methylene blue; Mol. weight: 320

Here we observe two dialkylated "LSD-tails" each of which has 4 C atoms (instead of 3, in LAE and LSD) between the primary amino group and the N-atom of the ring.

Before considering some of the structural characteristics of SKF-501 which displayed a high affinity for wool among all the compounds tested in this study and under our experimental conditions, let us draw attention to the findings of Harvey and Nickerson, 1953, which show that compounds of the Dibenamine type, including SKF-501, might occur in the body rather in their ethylenimonium form; these authors also have shown that such a form exerts the same adrenergic blocking activity as the original configuration.



SKF-501



ethylenimonium form of SKF-501
Mol. weight: 314

Summarizing: increasing absorption (higher degree of specificity for wool protein) of basic (cation-active) drugs is accompanied* by the following structural features: (*a*) increased grade of alkylation on the primary amino group, the latter which may be present as quaternary N, in vivo, (*b*) increasing number of such amino-groups, (*c*) increasing number of C atoms (up to 4) between the primary amino group(s) and the neighbouring N of the nucleus, (*d*) the presence of two hidden "LSD-tails" and (*e*) a molecular weight around 320 seems to appear also as one of the characteristics of basic drugs displaying a high affinity

* Among other factors disregarded in this report; further factors, see Fischer and Larose, 1952b.

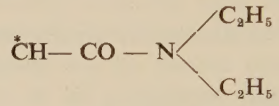
for wool. Some of the aforementioned common structural features of LAE, LSD, methylene blue and SKF-501 remind us that among the phenazathionium compounds substitution in the amino group (alkylation) is accompanied by an increase in basicity; the latter characteristic, however, might be regarded only as one of the factors influencing the affinity of our basic compounds for wool (Fischer and Larose, 1952b).

Since the following data, kindly supplied by the courtesy of Professor E. Rothlin, indicate that there is no increase in basicity if comparing LAE with LSD:

pK_b in H_2O of	Mescaline ..	4·25
	LAE	7·17
	LSD	7·12

the higher affinity for wool of the latter is due to other factors.

There are numerous problems as well as questions arising in connection with the above speculations; e.g. is the optically active $\overset{*}{C}$-atom and its adjacent structural part, the



grouping involved in the highly specific action of LSD? Such questions remind us of the limitations of wool in this study, since (*a*) wool protein might be regarded only as a *model* of the protein component of the target organ(s) playing a part in the production of model psychoses by drugs, (*b*) affinity (sorption) of a drug for protein is only *one* of the *factors* considered up to now in this report.

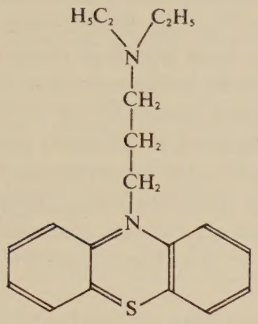
Another factor is suggested by the finding that thioglycolic acid, used in the permanent waving of hair, precipitated a reversible psychotic experience in a healthy individual (Lucy, 1953). Since the above compound alters the cystein part of proteins, namely their –S–S– bonds, one aspect of its mode of action might be a direct one, namely alteration (Schöberl, 1953) of the protein component of the receptor (target) organ itself.

Another problem refers to the adrenergic blocking activity of compounds and the possible relationship of such activity to those common structural characteristics concomitant of drugs exerting high affinity for wool protein.

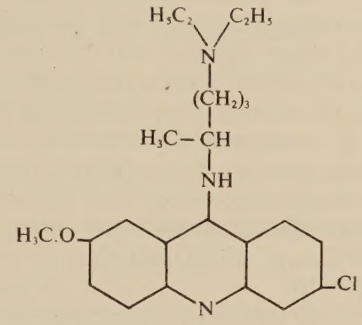
Finally let me digress in the direction of a very general speculation on biological activity. It might be that different levels of affinity for (wool) protein correspond to apparently different biological activities as viewed by different specialists in biology. Methylene blue, e.g. is a dyestuff capable of staining, among others, the ends of living nerves, it is an analgesic, an antimalarial and an antiseptic, etc.; phenothiazine is an anthelminthic and the base substance of drugs with antihistaminic, fungicidal, adrenolytic, antiemetic and "artificial hibernation"-inducing activity, etc. We could multiply such examples. It seems that derivatives of a compound displaying high affinity for (e.g. wool) protein, exert various biological activities according to the degree of specificity they display toward the available receptors, some of them apparently containing a protein component structurally related to wool.

High affinity for wool of basic compounds seems also to be associated with very potent biological activity. This activity is evidenced by the small dose of compounds required to exert their activity; e.g. the affinity of the biologically highly active Largactil for wool is high, i.e. 5·3 millimoles·10^{-2} per gm. wool.

The low affinity of Atabrine for wool (0·9 millimoles·10^{-2} per gm.) on the other hand explains why it has to be administered in high dosage and for a prolonged period.



Chlorpromazine (Largactil)
Mol. weight: 318.5



Atabrine (Mepacrine)
Mol. weight: 435.9

B. Related to Factors Aggravating and Preventing Model Psychoses Caused by Drugs

Our results as well as previous (Fischer, 1953b) and present reasonings imply the possibility:

First, that stress situations causing sympathetic stimulation and overactivity (e.g. the shock phase of the General Adaptation Syndrome (G.A.S.) of Selye, or administration of 1 mg. of atropine prior to LSD (Forrer and Goldner, 1951)) might diminish that dosage of a drug which is required to cause model psychosis at rest. Analogously it is possible to decrease the intensity of a hallucinatory experience, e.g. caused by LSD if the volunteer is successfully influenced psychologically as to feel freer from anxiety previous to the administration of the drug (Hyde, 1954; Stefaniuk, 1953). The latter observation which we would call an "LSD minus stress"-experiment, confirms our recently published views about model psychoses (Fischer, 1953b).

A similar but even more complete freedom from anxiety and its concomitant sympathetic overtonus might be achieved by administration of drugs causing "artificial hibernation" (Weese, 1953; Laborit, 1953; Benitte, 1953), see Largactil. Such drugs prevent the mediation of the stress response and thus result in a "pure" adrenergic blockage. No model psychosis will result in this case. Such an explanation favours also the understanding of the observation of Walter-Buel, according to whom only one-fifth of *hypertensive* patients, apparently those with high adrenalin and noradrenalin levels to which they were not adapted, experience a model psychosis after Dibenamine, another "pure" adrenergic blocking agent. These patients might also be regarded as being under the stress of their milieu interieur and thus displaying anxiety and sympathetic overtonus. Hence *stress* and *adrenergic blockage* seem to be essential components for the precipitation of model psychoses. Such reasoning means implicitly that drugs causing model psychosis, the latter which might be due to a reversible disturbance of the integration between diencephalon and cortex resulting in a lowered reality threshold, may act by exerting (*a*) a *sympathetic overtonus* due either to a counterregulation after administration of an adrenergic blocking agent, or to the high dosage of the agent in question thus containing also an unspecific alarming stimulus (Fischer, 1953b) and (*b*) an *adrenergic blocking activity*. An analogy: those patients whose hypertension is of psychogenic nature

and who are characterized by a definite sympathetic overtonus, become mentally disturbed if the symptoms of their hypertension are relieved ("adrenergic blockage") by psychotherapy (Draper, 1935).

Second, that persisting stress situations causing first sympathetic and then parasympathetic stimulation and overactivity (e.g. the counter-shock phase of the G.A.S.) might increase that dosage of a drug which is required to cause hallucinations at rest. Such a reasoning would fit in the manifold observations confirming the strange phenomenon of different reactivity of a schizophrenic towards e.g. methedrine if the drug is administered in different periods of the schizophrenic process; such a different response might be explained by assuming that the schizophrenic—due to his genetically inherited low threshold towards stress—is permanently under stress during the active phases of the schizophrenic process (Williams, 1953) and thus in one or another phase of the G.A.S. (Fischer, 1953b).

Third, that simultaneous administration of one of the four drugs (which cause model psychosis) together with an adrenergic blocking agent may intensify the psychotic experience, and

Fourth, that administration of certain compounds with a high affinity for (wool) protein might prevent by means of competitive inhibition the production of hallucinations caused by LAE or LSD.*

Summary

Factors involved in the production of a reversible model psychosis caused by either 500 mg. mescaline, 100 mg. methedrine, 1 mg. lysergic acid monoethylamide or 100γ lysergic acid diethylamide respectively, are considered.

Wool is used as a model for the protein component of the target organ(s) involved in the production of model psychoses.

Increasing affinity (absorption) of the above-mentioned compounds to (wool) protein goes parallel with the decreasing amounts of the same drugs necessary to cause a model psychosis of similar intensity and duration.

Increasing affinity (absorption) of the above mentioned compounds for (wool) protein goes parallel with the decreasing amounts of the same drugs necessary to cause a model psychosis of similar intensity and duration.

Sympathetic overtonus and subsequent adrenergic blockage are apparently among the factors contributing to the precipitation of a model psychosis.

Speculations are made (*a*) relating chemical structure to biological activity, (*b*) as to the possible aggravation, amelioration and prevention of drug-produced model psychoses.

Acknowledgments

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* A preliminary experiment (to be published with N. Agnew) seems to indicate that methylene blue for example, a weak adrenolytic compound (Marquardt and Schumacher, 1953) but displaying higher affinity for wool than LSD, is able to reduce by approximately 40 per cent. the intensity of an 80γ-LSD experience. The 0·15 gm. methylene blue is administered intragluteally prior to the LSD. These experiments are being continued using compounds displaying even higher affinity for wool than methylene blue. To date Diparcol (Diethylaminoethyl-N-dibenzoparathiazine hydrochloride)—affinity for wool 5·5 millimoles·10^{-2} per gm. wool—appears to be the most effective compound in blocking out LSD symptoms.

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THE EFFECT OF ELECTRO-CONVULSIVE THERAPY ON THE PSYCHO-GALVANIC RESPONSE

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Introduction

Though electro-convulsive therapy (E.C.T.) is one of our most useful treatments, its mode of action is still largely unknown, and this ignorance is preventing us from making it more successful and more widely applicable. Among its possible modes of action is the possibility of its having some "activating" action on the basal, and more particularly on the hypothalamic, structures. Such activation might be expected to show in the psycho-galvanic response (P.G.R.), and we have therefore investigated something of the relationship between them. Many of the facts that would justify this investigation need not be given here as they have been reviewed in previous publications (Ashby and Bassett, 1950; Ashby, 1952(b)).

Knowledge of the effect of E.C.T. on the P.G.R. may at least help in establishing a primary orientation in the question of how E.C.T. acts therapeutically; for at present the possibilities range from an action by some shock-like effect on the pituitary and other endocrines, through events in the psycho-analytic mechanisms, to a randomly distributed effect on the cerebral cortex, forcing disorganization and subsequent re-integration (Roth, 1952; Ashby, 1952(a)). Study of its effect on the P.G.R. may help to give such an orientation, and we decided therefore to follow the P.G.R. over the weeks of treatment, particularly with the aim of seeing whether the treatment would lead to any sustained increase in the patient's responsiveness.

Since we wished to follow the P.G.R. over some weeks, and therefore wished to get as smooth a curve as possible, we decided not to evoke the response by the use of emotionally toned words, since their effects might by expected to fluctuate widely, but to use more or less direct physical stimuli whose properties could be controlled within narrow limits. We therefore used such stimuli as a flash of light to the eye. We wished, however, to explore something of the subject's "higher" reactions to his environment, so we decided also to test his response to the merely threatened application of the physical stimulus, bringing the lamp into position but not making it flash. Various stimuli were used, as will be described below.

It was clear that the chief difficulty in the interpretation of the results would lie in assessing the effect of habituation—the universal tendency of the reacting organism to react less and less as a series of non-injurious and repetitive stimuli are given. Repetition there had to be, for the later results must be comparable with the earlier.

Consideration suggested that it would be necessary to compare how the P.G.R. changed during E.C.T. with how it changed in other groups that were comparable but which did not have the treatment. Two other groups were therefore tested, as will be described below.

A number of minor factors had to be considered, but they can be described as they become relevant. We can now proceed to a description of the method used.

Apparatus and Tests

Our apparatus and method of testing followed the same basic form that we had used previously (Ashby and Bassett, 1950). The details need not be given here as they were given in the previous publication. Briefly, the subject's resistance was measured by a Wheatstone bridge and microammeter, the hands being immersed in saline. Before and after each stimulus the subject's resistance was measured, and the maximal deviation caused by the stimulus was noted.

The stimuli consisted of four fairly strong peripheral stimulations:

1. A pinch to the lobe of the left ear by a clip of standardized strength;
2. A smell of 2 per cent. (v/v) ammonia;
3. A brief flash of light from a "Photoflood" lamp held at fifteen inches from the eyes;
4. A touch on the right conjunctiva by a wisp of cotton wool.

At each session, each of these was given both by direct application and by threat; in the latter case the apparatus for the peripheral stimulation (clip, lamp, etc.) was brought near the patient so that he knew that stimulation was about to occur, but the actual stimulation was not given. (The two sets of stimuli will be distinguished below by the adjectives "Real" and "Threatened".) So that the subject should not know whether any given presentation was to be real or threatened, the eight stimuli were given, at each session, in random order, the actual order being obtained by the use of a table of random numbers (Fisher and Yates, 1938).

Subjects were tested over five weeks, usually for a week before commencing E.C.T. and then during the first four weeks of treatment. They were deliberately tested with a variety of intervals between convulsion and test, and were tested at various times of day, so that the effects of these factors could be assessed. So far as the clinical and administrative requirements allowed, a similar routine was followed for all. (Evidence will be given below suggesting that the minor variations were without significant effect on the conclusions drawn.)

The Subjects

The thirty-nine subjects were drawn from three groups:

1. Normal persons, volunteers from the staff (referred to below as "Normal");
2. Patients who did not receive E.C.T. (referred to below as "Untreated");
3. Patients who received E.C.T. (referred to below as "Treated").

Subjects of the first two groups were, of course, required as controls for those in the third. In all three groups, the majority were women.

(1) *The "Normal" Group*

Of the seven volunteers from the staff of the hospital, two were men and five women. The range of their ages was from 19 to 50. None, as far as is known, had had any psychiatric disability and all were in good physical health. They were studied chiefly in order to show the amount of habituation normally developed during the five-weeks' course of testing.

(2) *The "Untreated" Group*

The sixteen subjects in this group were all in-patients, three being men and thirteen women. The range of their ages was from 17 to 60. They were all sufficiently co-operative to undergo the five weeks of rather monotonous testing and they were all clinically such that they would have had E.C.T. had not some extraneous factor prevented it. They were therefore closely similar to the group of patients that did have E.C.T. Clinically they included various conditions, chiefly depressions. Six of them received E.C.T. after the testing had been completed.

This group was required generally to act as control to the "Treated" group.

(3) *The "Treated" Group*

The sixteen subjects that formed this group, ten women and six men, were all in-patients. The range of their ages was from 17 to 62. The criterion for inclusion in the group was that they should be sufficiently co-operative and that E.C.T. should be commenced a week after the commencement of testing. Clinically, the group closely resembled the "Untreated".

It was this group's reaction to E.C.T. that formed the subject of the work.

Scale of Measurement

Experience over some weeks of preliminary testing showed that the responses to the four different stimuli (pinch, smell, flash and touch) were highly correlated. As this meant that the distinctions between them were hardly worth preserving, we decided that the basic "response" should be some function of the average of the four separate responses, the distinction between "Real" and "Threatened" being retained. The four responses (in divisions of the galvanometer deflection) were therefore averaged at once to give the basic "response". The question then arose, when response was to be compared with response, which scale would relate the responses most suitably.

The best method of converting the response into numerical form has been the subject of discussion for a number of years. It was recognized long ago that the size of the P.G.R. was dependent upon, among other factors, the initial resistance of the skin, and that a direct comparison of the deflections given on two different occasions was therefore not appropriate. To allow for this, the size of the response was often expressed as a percentage of the subject's mean reaction to all stimuli. Later, Hunt and Hunt (1935) compared five different ways of scoring the response; they found that the intercorrelation between the five methods approached unity, but nevertheless concluded that the absolute number of ohms change was preferable. Darrow (1937) suggested that a better method would be the use of a measure based on the logarithm of the conductance. Since then, the question has been studied thoroughly by Haggard. He tested a variety of functional forms on abundant and suitable material, and used modern statistical techniques to find the best. His views developed in two stages. He first (Haggard and Garner, 1946) showed that if the resting ohmic resistance is x ohms and the extreme resistance during the response is y ohms, then the function

$$\frac{\log_{10}(x-y)}{x} \quad \ldots\ldots \text{(A)}$$

was independent of the initial skin resistance over a wide range, even when the maximal responses were provoked by strong electrical shocks. He also showed that the residual variance of this expression was satisfactorily constant at the

different levels of skin resistance, and also at the different levels of mean response.

He must, however, have been dissatisfied with this form for he later (1949) made further studies with new forms. Among the forms studied were the logarithm of the change in conductance

$$\log\left(\frac{1}{y}-\frac{1}{x}\right) \quad \ldots.(B)$$

and the change in the logarithm of the resistance

$$\log y - \log x,$$

which is the same, of course, as

$$\log\frac{y}{x} \quad \ldots.(C)$$

He came to the conclusion that form B was best.

Haggard, however, omitted zero responses from his calculations, and studied the best conversion of the remainder. In our work a zero response must be considered meaningful, and therefore as probably best not ignored. The inclusion of zero responses, however, makes his form B unusable, for when the response is zero form B becomes $-\infty$, a quantity that cannot be used in the subsequent arithmetic. His function C, however, was also shown by him to remain constant when, with constant stimulation, the skin resistance was made to vary over a range of 1,000 to 8,000 ohms. As, in addition, it transforms a zero response to zero, we used it to convert the skin resistance and observed deviation to a scale suitable for statistical treatment. For its computation a nomogram was constructed, allowing the value of the function to be read off when the subject's basic resistance and the number of divisions of deflection were known.

A minor question to be decided was whether to take account of the deflection's direction. Thus, if the responses were +5 and −5 divisions, should we take their simple average, and regard the "average response" as zero, which seemed artificial in this context, or should we take the average of their absolute values, and consider it to be 5? After consideration we decided on the latter. (In fact the decision mattered little as almost all responses were in the same direction.)

For convenience in computation we multiplied the function C by 1,000, and this multiple is the number used in the Figures below. So a value z in a Figure means that

$$\frac{y}{x} = \text{antilog}_{10}\left(\frac{\pm z}{1{,}000}\right);$$

thus "25 logarithmic units" means that (if the resistance fell)

$$\begin{aligned}\frac{y}{x} &= \text{antilog}_{10}\,(-0{\cdot}025)\\ &= \text{antilog}_{10}\,\bar{1}{\cdot}975\\ &= 0{\cdot}944,\end{aligned}$$

i.e. that the skin resistance fell by 5·6 per cent.

This measure, although more complex than a direct record of the change in ohms, has the advantage that both its size and its residual variance are almost entirely independent of the resting level of the skin resistance.

With these methods were tested our series of patients, the actual testing being done throughout by one person (M.B.). The factors that were deliberately varied in order to explore the causal relationships were:

1. The sensory mode of the stimulation.
2. Whether the stimulation was real or threatened.
3. Whether the subject was psychiatrically normal or not.
4. The time of day of the test.
5. The time that had elapsed since the last convulsion.
6. The time that had elapsed since the testing or the E.C.T. had commenced.

Results

In this investigation we were hampered by the difficulty, common when working with patients, that the conditions could not be controlled and selected as they can with animals. The details of the testing could be controlled, but not the many factors relating to the patient's illness and recovery. We have been forced therefore to depart to some extent from the proper balance of test and control, deviating from the arrangement in which the factors would vary with strict orthogonality. When the orthogonality is incomplete, the statistical testing and the interpretation of the results become complex and less reliable.

Our results deviated, in their entirety, only slightly from the orthogonal, so we were often able, in the statistical analysis, to take a subset of our full results and thereby to get a group over which the factors varied with exact orthogonality. Where such a subset existed we have used it. Where none existed we have either used the next best approximation or have tested the factor over more than one set, so as to minimize any risk of error. In our description of the results below, we have confined our statements to those which we are satisfied are free from any serious risk of error.

The results will be given for each of the groups (normal, untreated, and treated) in turn, and then we will consider the point of the investigation, the comparison of group with group.

The "Normal" Group

Figure 1 shows how, on the average, the normal subjects reacted to the

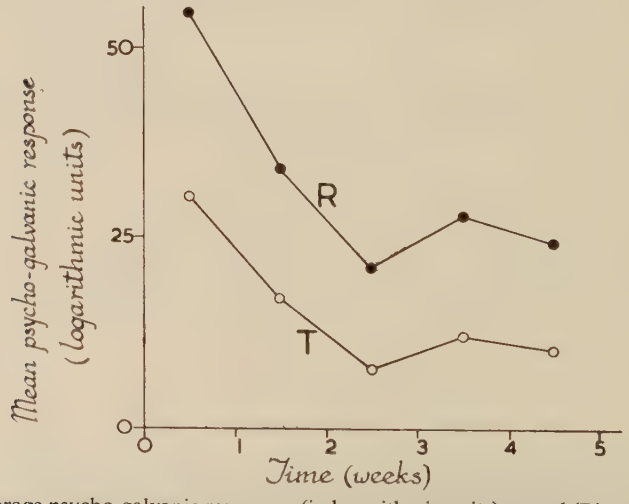

FIG. 1.—Average psycho-galvanic responses (in logarithmic units) to real (R) and to threatened (T) stimuli over five weeks of testing. Normal subjects.

repeated testing; habituation is marked. The response fell over the first few weeks and then settled at a basic level. The change with time is significant statistically, for P is less than 0·001 when the averages are compared over the five weeks. The curves for Real and Threatened stimuli are similar, with the value for Real usually about twice as large as that for Threatened. (The difference between the mean heights, allowing for Time, is significant with $P<0·001$; there is no significant difference between the regressions: $P>0·05$.)

The average responses given at various times of the day by this group were:

	10 a.m.	12 noon	3 p.m.
Real	30·3	35·4	28·7
Threatened	15·0	17·5	14·6

The small differences, for given type of stimulus, are not significant statistically ($P>0·05$). Evidently time of day is not an important factor in this group.

The "Untreated" Group

Figure 2 shows how this group responded to the continued testing. Again the initial fall is marked; it is also significant as a regression, for P lies between

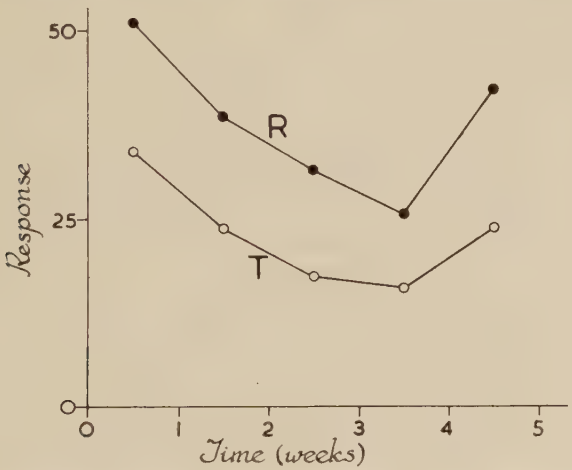

FIG. 2.—Average responses to real (R) and to threatened (T) stimuli over five weeks of testing. Untreated subjects.

0·01 and 0·001. The regressions for R and T do not differ significantly. The increase of response in the fifth week has an origin that is discussed later.

The difference in mean response between R and T is again significant ($P<0·001$).

The average responses given by this group at various times of the day were:

	10 a.m.	12 noon	3 p.m.
Real	52·9	42·3	30·6
Threatened	36·7	26·7	16·0

In this group the mean responses differ significantly with the same type of stimulus (P is between 0·01 and 0·001), contrasting with what was found in the Normal group.

The "Treated" Group

This group, it will be recalled, were tested while undergoing their course of treatment, which commenced after the first week's testing. As in the other two

groups, the response to Real stimuli was always about twice as large as that to Threatened (Fig. 3). The difference between them was significant with $P<0{\cdot}001$.

The average responses given by this group at various times of the day were:

	10 a.m.	12 noon	3 p.m.
Real	33·3	41·8	36·2
Threatened	21·2	24·4	23·9

None of the changes is significant, a matter of some importance, as it might have been thought that our practice of giving E.C.T. in the morning would introduce a serious bias.

For the same reason we also studied how E.C.T. affected the P.G.R. within a few hours of the convulsion, for this knowledge was necessary in order to plan the general form of the investigation. Observations were therefore made of the patient's responses at three sessions held on the same day as the convulsion at $\frac{1}{2}$, $2\frac{1}{2}$, and $5\frac{1}{2}$ hours after it. Six patients were studied in this way; their average responses were:

	$\frac{1}{2}$ hour	$2\frac{1}{2}$ hour	$5\frac{1}{2}$ hour
Real	30·8	30·5	31·0
Threatened	20·2	19·9	22·3

Analysis of the variance showed that no significant difference exists between the responses at the times within the range covered. It is of interest to notice that E.C.T. has little effect on the P.G.R., even when the test is made only half an hour after the convulsion. (The skin resistance is usually much less, but the functional form C makes the appropriate allowance for this.)

This lack of effect over a few hours is confirmed when, in the Treated group, the average size of the response on the days in which a convulsion was given is compared with the average size on the days without convulsion. For real stimuli the effect is statistically insignificant, while for threatened stimuli the difference gave $P=0{\cdot}05$. On the whole, the effect is slight if it exists at all.

This being so, the factor "time of day at which the test was conducted" can be eliminated as ineffective within our system of testing.

We now come to the point of the experiment. Figure 3 shows the actual responses made by those in the Treated group, the commencement of the treat-

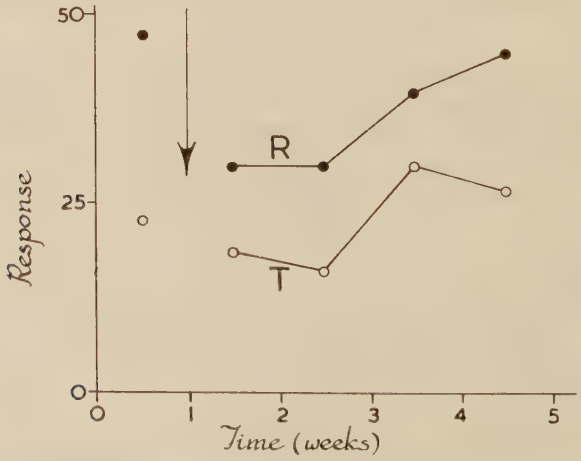

FIG. 3.—Average responses to real (R) and to threatened (T) stimuli over five weeks during which a course of E.C.T. was begun (at the arrow).

ment being at the arrow. Before discussing its significance, however, we must consider the main complicating factor.

Habituation

We now come to the question of how much habituation is occurring in the Treated group while the course of E.C.T. is being given and while the E.C.T. is having its (unknown) effect on the P.G.R. Such habituation is, of course, tending to mask the effect we are trying to discover.

First the facts. Figure 3 shows how the Treated group changed, week by week, in their responses to real (R) and to threatened (T) stimuli. The two isolated points on the left show the responses before the treatment was started, and those to its right show the combined effects of the treatment and of the habituation.

An approximate assessment of the effect of the E.C.T. on the response can be made by comparing the curves in Figure 3 with those in Figures 1 and 2 (the curves for the Normal and Untreated groups). Habituation is most clearly seen in the Normal group; and inspection would suggest that the Treated group was showing some increase, in the later weeks, over the level produced by habituation. Some test of statistical significance is, however, required. Consideration suggests that the fitting of some elaborate curve, some high order polynomial, would be of dubious advantage, and a low order polynomial (straight line or parabola) is obviously inappropriate. The most suitable method seems to be to compare simply the averages of the three groups at each of the five weeks, giving five independent tests. Though somewhat insensitive, this method has the advantage of indicating significance only if the significance is unquestionable.

The results for the five weeks are as follows:

Week 1: The average *R* responses in the three groups show no significant differences; neither do the average *T* responses. (This homogeneity confirms our impression that the three groups of subjects were, so far as their P.G.R.s are concerned, sufficiently uniform before the E.C.T. was applied.)

Week 2: (As Week 1.)

Week 3: As Week 1 in the *R* responses. In their *T* responses, *P* was between 0·05 and 0·01, the responses in the Normal group being lower than those in the other two. (The difference is probably of little importance.)

Week 4: As Week 1 in the *R* responses. In the *T* responses, *P* was between 0·01 and 0·001, the responses in the Treated group being higher than those in the other two groups. This confirms, as statistically significant, the visual impression that the curve runs high in the Treated group (Fig. 3).

Week 5: In the *R* responses, *P* is less than 0·001; in the *T* responses, *P* is between 0·05 and 0·01. In each, the response is significantly larger in the Treated group.

The tests are thus decisive in showing that some real effect is tending to cause a rise in the later weeks, the value rising above that to which the response would sink by simple habituation. We now have to consider whether the effect is due to the E.C.T. or to some correlated factor.

The "Recovery" Factor

We were interested in the question whether measurement of the P.G.R. would be of value for prognostic purposes and we therefore separated our results into two groups according to whether the patients did, or did not subsequently recover, and we did this of course, in both the Treated and the Untreated groups. We found that the size of the P.G.R., particularly in the fourth and fifth weeks of testing, was markedly dependent on this factor of whether or not recovery followed eventually. The results were therefore reanalysed completely. The full details need not be given here, as a new and more thorough investigation of the phenomenon is now in progress. We can, however, summarize the facts so far as they are necessary.

To display the relation more clearly, the responses to real and to threatened stimuli can be combined to a single "response" S by forming the linear function (or weighted average)

$$S = \frac{1}{3}(R+2T),$$

where R and T are the responses to real and to threatened stimuli. The loss of the distinction is of no importance here since the various parts of the investigation (e.g. Figs. 1, 2 and 3) have shown that the two responses have no individual peculiarity in their relations to the other factors.

The subjects in the Treated and Untreated groups were divided into Recovered and Not-recovered, the criteria being:

1. In the Treated group, the Recovered were those, and only those, who were discharged as "recovered" or "improved" within six weeks of the end of the convulsive treatment;
2. In the Untreated group, the Recovered were those, and only those, who were discharged as "recovered" or "improved" within 12 weeks of admission.

Examination of the groups showed that they were sufficiently well balanced for age, sex, and clinical condition to be comparable.

Figure 4 shows, by the contrast between the continuous (————) and the broken (– – – – – – –) lines, how the Recovered group differed from the Not-recovered in their responses (respectively) as time progressed. The

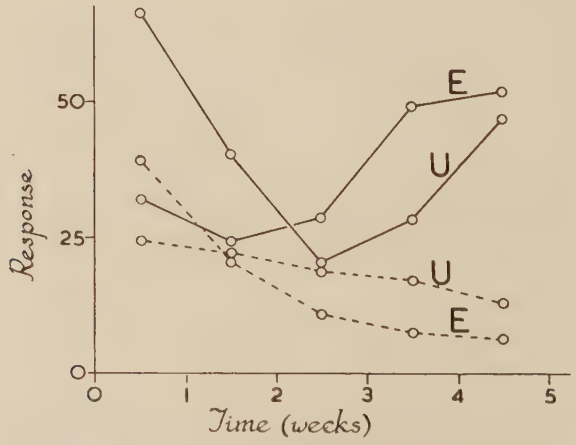

FIG. 4.—Average responses in the groups Recovered (————) and Not-recovered (– – – – – – –) over five weeks of testing. Curves for the Treated (E) and Untreated (U) groups are shown separately.

results are shown separately for the Treated (E) and the Untreated (U) groups; it will be seen that they are in substantial agreement.

This visual impression was confirmed by an analysis of variance over the forty averages given by the forty combinations of the factors:

1. Between weeks (4 degrees of freedom).
2. Whether Recovered or Not-recovered (1 d.f.).
3. Whether Treated or Untreated (1 d.f.).
4. Whether Real or Threatened stimuli were used (1 d.f.).

(The latter distinction was restored as a check on whether any significant difference existed.)

Since the analysis of variance is decisive in this question, it is given in full.

TABLE

*Analysis of variance according to the factors as numbered in the text. First order interactions represented thus: 2/4. Under "Significance", * means "significant at the 5 per cent. level", and ** means "significant at the 1 per cent. level."*

Variance	D.F.	Sum Sq.	Mean Sq.	*F*	*P*	Significance
Between weeks ..	4	2,272.	568.	3·79	0·02	*
Recovery	1	4,494.	4,494.	29·9	0·001	** (a)
Treatment	1	73.	73.	—	—	0 (b)
Real or not	1	2,722.	2,722.	15·1	0·002	**
1/2	4	1,484.	371.	2·47	0·1	0
1/3	4	287.	72.	—	—	0
1/4	4	226.	56.	—	—	0
2/3	1	5.	5.	—	—	0
2/4	1	29.	29.	—	—	0
3/4	1	4.	4.	—	—	0
Higher order interactions ..	17	2,558.	150.	—	—	—
Total	39	14,154.	—	—	—	—

The factors are numbered for convenience as in the list just given. The significance of (a), in the right-hand column, and the insignificance of (b) are decisive in showing that it is the factor 2 ("Recovery"), and not factor 3 ("Treatment"), that correlates with the size of the response. The remainder of the table shows that no interaction was significant, so there is no reason to suspect that the relationships are complicated.

It seems therefore to be clear that *E.C.T. has little or no direct effect on the size of the P.G.R.*

DISCUSSION

So far as we can trace, there seem to have been no previous measurements of the effect of E.C.T. on the P.G.R. with which our results can be compared. Solomon *et al.* (1939) found that the P.G.R. was increased in those patients who recovered after metrazol or insulin—a finding compatible with ours. Funkenstein *et al.* (1950), though not working with the P.G.R., had similar results when testing the reactions of patients, especially those who had recovered after E.C.T., to adrenaline. They found that whenever the clinical state of the patient changed with E.C.T. autonomic changes were detectable. They also came to the conclusion that patients' responses to E.C.T. correlated better with their responses to test injections of adrenaline and mecholyl than with their diagnostic category.

With regard to our own results, so little is known of the mechanism underlying the P.G.R. that only rather broad deductions can be made in regard to the question of how E.C.T. acts therapeutically. It is clear that our results must be regarded as unfavourable to those theories of E.C.T. that regard its action as being chiefly on some emotional factor or on the physical basis of such a factor. Were E.C.T. to work by making active some thalamic or hypothalamic centre, or even by working through the pituitary and adrenals, some increase in the average responsiveness would probably be seen. Figure 4 and the Table, however, show clearly that any rise that might be suggested by Figure 3 is to be attributed simply to the fact that the Treated group contains an undue number of patients who recover and not to the treatment *per se*. E.C.T. in itself is having little effect.

If E.C.T. is having little effect on the functions related to the emotions and the P.G.R., our work would, indirectly, tend to support those who hold that the action of E.C.T. is mostly direct on the cerebral cortex, where it produces a temporary disorganization, so that the normal processes of integration, given a new start, have another chance of developing a more normal pattern of behaviour (Roth, 1952; Ashby, 1952(a)). The question is, however, too large to be discussed adequately here; we merely remark that our results give it some indirect support.

The most striking finding of the investigation is that the size of the P.G.R. tends to go up in those who are about to recover; but as the matter is now under investigation, its discussion can be postponed.

Summary

Continuing our investigations into the mode of action of electro-convulsive therapy, we have studied its effect on the psycho-galvanic response.

Four different stimuli were used. Each was given both directly and in symbolic form. The responses were tested at various times after the convulsion and were also followed week by week after the commencement of treatment. Normal subjects were used as controls, and so were patients of similar clinical type who did not have the treatment. The number of responses observed was over six thousand.

We find that:

(1) In general, the effect of electro-convulsive therapy on the psycho-galvanic response is small.

(2) The effect of habituation, as session follows session, is marked.

(3) Most patients who are about to recover show an increased response, whether the recovery follows E.C.T. or is spontaneous.

We consider that our results favour the theory that E.C.T. acts directly on the cerebral cortex.

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"CONTROLLED PROJECTION" RESPONSES OF DELINQUENT BOYS

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I. Introduction

The "Controlled Projection" Test of Raven is a method of collecting and studying the projection responses of children to a standard series of situations (Raven, 1951). In reports so far published, the technique has provided information on differences in the organizations of thought and conduct characteristic of different national, social and clinical groups, and on individual differences within these groups.

This investigation was carried out to establish the normal incidence of responses of delinquent boys, to compare these phantasies with the conventional responses of ordinary children, and to evaluate the type of material elicited by the test. To make the sample as representative of young delinquents as possible, subjects were selected from the whole juvenile range of 8 to 17 years, with degrees of criminal conduct ranging from a first offence to a subject who was on remand for a sixth offence. The sample was divided into two groups on a basis of chronological age: the Junior group consisted of 43 boys aged $11\frac{1}{2} \pm 1\frac{1}{2}$ years, and the Senior group 43 boys aged $14\frac{1}{2} \pm 1\frac{1}{2}$ years. Both age groups had a normal distribution for intelligence. All subjects were resident in a London Remand Home: 9 boys had been charged with their first offence, 9 had a record of three or more previous offences, and the remainder had a record of 1 or 2 previous offences.

II. Method of Comparison

1. In the Controlled Projection Test the principles on which responses are classified are determined by the investigator. Raven grouped according to "similar statements occurring in the records", beginning with the most frequent and ending with those which were unique in the sense that each was given by only one child. A child's first response was accepted, and other responses in so far as they qualified the first. This is the method followed here, except that similar *ideas* are classed together, because the reply was pursued if the investigator was not satisfied that the boy had understood the question or was ashamed of replying fully.

2. The responses of the whole sample were categorized before Juniors' and Seniors' responses were separated. Categories were labelled A, B, C. . . G on a basis of frequency of kind of response. Unique responses which could not be placed in any of these categories were labelled U.

3. No limit was put to the number of categories which might arise from the replies to one question. When standardizing the test with the data of normal children for general comparative purposes, Raven combined categories under a more general heading if "the results of the preliminary grouping produced more

groups than the average number of responses per group" (Raven, op cit.). Some of the test questions, however, touch on acutely-felt topics, and a constraint put on the number of categories could result in obscuring the clear way in which the phantasies fall into distinct classes.

III. Summary of Results

	Juniors	Seniors	Total
1. Once there was a boy			
(a) *What did he like doing?*			
A. Group Outdoor Sports	25	32	57
B. Schoolwork	10	2	12
C. Solitary Outdoor Activities	3	6	9
D. Stealing	2	1	3
E. Cinema	1	1	2
F. Eating	1	1	2
U. Woodwork	1	0	1
(b) *When he was playing, who did he like being with?*			
A. Friends of the same age and sex	33	35	68
B. Relatives	9	3	12
C. Me	1	1	2
D. Animals	0	2	2
E. Male adult	0	1	1
U. To be alone	0	1	1
(c) *Who did he not like being with?*			
A. Boys who thieve, quarrel, show off, or are dirty, rough, dishonest	34	29	63
B. Girls	2	3	5
C. His friends	3	2	5
D. No-one	2	2	4
E. Relatives	0	4	4
F. The Police or the Vicar	1	3	4
U. Unclassified	1	0	1
2. One day this boy went out with his mother and father and they got cross with him			
(a) *What was it about?*			
A. Disobedience	23	17	40
B. Being aggressive or disagreeable	9	12	21
C. Accident, e.g. losing money, soiling clothes, getting run over	6	4	10
D. He broke the law	2	6	8
E. He wanted toys	2	4	6
U. He drank dirty water	1	0	1
(b) *How did it end?*			
A. By forgiveness or atonement	12	14	26
B. Corporal punishment	13	13	26
C. Other punishment, e.g. sent to bed	9	10	19
D. He was sent away, e.g. to a Home	2	4	6
E. He ran away from Home	3	0	3
F. He got injured	1	1	2
U. Unclassified	3	1	4
3. One day his mother and father were cross with each other			
(a) *What made them cross?*			
A. Father blamed or punished the boy for no stated reason	19	11	30
B. The wages were insufficient, or Father had drunk them, or Mother had spent them unnecessarily	7	9	16
C. Something the boy wants or does	8	7	15
D. Domestic upsets, e.g. the dinner was burned	6	9	15
E. Mother punished or blamed the boy	2	4	6
F. Because Mother leaves Father	0	2	2
U. Unclassified	1	1	2

(b) *What happened then?*

A. Reconciliation	16	19	35
B. The boy is punished, or he runs away from home	10	6	16
C. Fighting between parents	7	5	12
D. Father leaves home	4	6	10
E. Mother leaves home	2	4	6
F. Mother and Father part	2	1	3
U. Unclassified	2	2	4

4. ONE DAY HE SAID TO HIS FRIEND, "I'LL SHOW YOU SOMETHING BUT YOU MUSTN'T TELL ANYONE BECAUSE IT'S A SECRET"

(a) *What did he show him?*

A. Animals, birds' nests	7	15	22
B. Camps, caves, tunnels, hideouts	7	13	20
C. Treasure, jewels, lead, money	13	6	19
D. Useless things; aeroplane parts, farthings	6	3	9
E. Useful things, e.g. knives, toys	5	0	5
F. Food	3	2	5
U. Unclassified	2	4	6

(b) *What did they do?*

A. Played there	16	28	44
B. Stole, damaged, or was informed on	13	7	20
C. Spent money or gave something away	7	3	10
D. Hid or buried something	2	2	4
E. Got frightened or was punished	1	2	3
U. Unclassified	4	1	5

5. ONE DAY HE HAD A FRIGHT. WHAT HAPPENED?

A. He got hurt, or nearly got hurt	23	22	45
B. He was caught stealing, or was informed on	10	6	16
C. Someone else got hurt, or nearly got hurt	3	6	9
D. He lost his camp, cat, dog, or mouse	3	2	5
E. Misfortune to parents	2	3	5
F. He saw something strange or terrifying	2	2	4
G. He lost or saw again the thing he stole	0	2	2

6. HE USED TO MAKE UP THINGS; SOMETIMES THEY WERE TRUE AND SOMETIMES THEY WEREN'T

(a) *He told the other boys one of his stories. What did he tell them?*

A. *Boastful stories*	12	19	31
That he was given or found money, relics, treasure, bicycles (12)			
That his father or ancestor is a hero and/or gives him gifts (10)			
That he had a treasure hidden away (4)			
That he found useless things (3)			
That he had a hideout (2)			
B. *Stealing*	11	6	17
He had stolen, would steal, or denied stealing (11)			
Someone else stole (5)			
He knew where stolen stuff was (1)			
C. Boastful or amusing events of everyday life	7	7	14
D. Frightening events	6	6	12
E. Orthodox fairy tales	4	4	8
U. Unclassified	3	1	4

(c) *One day he told his mother and father one of his stories—what did he tell them?*

A. *Stealing and Wrongs*	13	13	26
He had stolen, or would steal (4)			
He found something which he in fact stole (4)			
Someone else stole (2)			
He did something wrong (2)			
He didn't do or wasn't going to do anything wrong (11)			
Someone else did something wrong (3)			

B. *Harm*	14	9	23
He got hurt or nearly got hurt (10)			
A man was poisoning him (1)			
Someone else got hurt or killed (11)			
Mother was ill (1)			
C. *Boastful*—he had done or would do something brave or clever	4	12	16
D. Jokes and everyday events	4	5	9
E. Dramatic events, e.g. fighting between adults ..	4	1	5
F. He was going to be put away, or he wanted to run away	1	2	3
U. Unclassified	3	1	4
7. (a) *When this boy went to bed, what did he think about?*			
A. *Everyday events* concerning the	18	25	43
Past (11)			
Future (32)			
B. *Guilty thoughts*	10	13	23
Lies, truancy, theft or contemplated theft (12)			
Regret for unspecified wrongs (8)			
Regret for masturbation (1)			
Doing good the next day (2)			
C. *Frightening thoughts*	5	3	8
Loss of a friend or dog (3)			
Getting hurt or frightened (3)			
Being put away (1)			
Of an absent mother (1)			
D. *Family*	6	1	7
Mother and/or father (5)			
Prayers for relatives (2)			
U. Unclassified	4	1	5
7. (b) *One evening he cried. What was the matter?*			
A. *Injuries or ills to himself*	16	16	32
By an accident (17)			
By someone's intention (15)			
B. *Fearful thoughts*	14	11	25
Burglars, shadows, nightmares (11)			
Of being sent away (4)			
Of being reported to police or school (3)			
Of a parent leaving home (2)			
Of having no friends left (4)			
Of losing a pet (1)			
C. *Guilty thoughts*	9	8	17
Injuries to relatives (7)			
Injuries to others (3)			
Told his parents lies (5)			
Been naughty (1)			
Broke the toy he stole (1)			
D. Punishment (non-corporal) by parents	2	7	9
E. He wanted to be away from parents	2	1	3
8. (a) *When he fell asleep what did he dream about?*			
A. *Attainment*	16	22	38
Of material object or pleasant event (19)			
Excelling as a boy or man (19)			
B. *Guilty or Frightening Dreams*	21	16	37
Harm to himself (22)			
Guilt over past or future misdeeds (6)			
Stealing or lies (3)			
Disliking his mother (2)			
Harm to others (4)			
C. *People*	2	2	4
Relative or friend			

D. *Sexual dream*	1	1	2
U. Unclassified	3	2	5
8. (b) *He woke up in the night. What made him wake up?*			
A. *Guilty dreams or nightmares*	16	24	40
Injury to himself (31)			
Injury to relatives (3)			
Injury to others (3)			
His mother forgiving him (1)			
His parents would believe his lies (1)			
Of the Police (1)			
B. *Noises, involving fear*	15	5	20
Of burglars (3)			
Of an imagined injury (5)			
Over an unspecified cause (5)			
Waking with fear, proving harmless (7)			
C. *Noises, harmless*	8	11	19
D. *Dreams* of parent, friend, dog	2	1	3
E. *Illness*	1	1	2
U. Unclassified	1	1	2
8. (c) *If he said what he most wanted it would come true. What did he say he wanted?*			
A. *Playthings*, e.g. bicycles, cars	23	19	42
B. *Treasure*, e.g. gold, magic lamp, money, sweet shop, orchard	9	4	13
C. *Forgiveness*, e.g. not to thieve, lie, get caught, get sent away; to tell the truth, to be forgiven	5	6	11
D. Happiness and wealth of family	0	5	5
E. Animals	1	3	4
F. Parental re-union	0	3	3
U. Unclassified	5	3	8
8. (d) *He was given a thousand pounds. What did he do with it?*			
A. Bought things and saved some	33	29	62
B. *Reparation*	7	11	18
Gave it all to parents (11)			
Repaid parents for their trouble (1)			
Restored stolen property (1)			
Took it to mother at Police Station (1)			
C. Was swindled or robbed	2	0	2
D. Bought cigarettes or went to cinema	0	2	2
U. Unclassified	1	1	2
9. *Does he want to grow up? What does he want to do when he grows up? Does he want to stay young?*			
A. *To grow up*	33	29	62
And work (58)			
To do as he liked (2)			
To be popular (1)			
B. To stay young	8	11	19
C. To grow up so as not to commit his crime again	1	1	2
U. Unclassified	1	2	3
10. THAT'S THE END			
(a) *What do you like about the boy in the story?*			
A. *Do like the boy* (guilt motive)	15	18	33
For being sorry for past transgressions, for promising not to transgress again, for thinking of Mother and Father first, for not playing with bad boys, for giving all the money to mother back again			
B. *Don't like the boy*	8	10	18
Anything about him, for his thieving, for his lying, except when he told the truth or gave the money back			

C. *Do like the boy* For his sportsmanship, kindness, generosity, etc.	7	10	17
D. Question not understood	10	5	15
E. *Like him* because he told lies	2	0	2
F. The boy is me	1	0	1
(b) *What do you dislike about him?*			
A. Tells lies	9	16	25
B. Steals, causes "trouble" to parents, robs birds' nests	8	8	16
C. Nothing	10	4	14
D. *Normal faults*, e.g. bad manners, disobedience, etc.	6	6	12
E. Agressiveness (exaggeratedly so)	5	3	8
F. Question not understood	2	2	4
U. Unclassified	3	4	7
(c) *Is he the same as you? In what way? (Or, in what way isn't he?)*			
A. *Unlike* because the boy in the story is *less* dutiful, truthful, kind, honest	13	17	30
B. *Like* the same (12), nearly the same but differing by a detail (9), the same except for events occurring in the story (5), like in the face and no difference (1)	12	15	27
C. *Unlike* in appearance only, or in events occurring in the test questions, or in a particular toy wanted (13), or where he lives or is richer (13)	9	9	18
D. *Unlike* because the boy in the story is *more* honest, truthful, kind, or less troublesome	4	1	5
E. Question not asked	2	1	3
F. He is me (2), or, he is another real boy (1)	3	0	3

IV. Discussion of Results

1. *Interests, Friends, Aspirations.* (Qs. 1, 4, 6a, 6b, 8c, 8d, 9)

The boys' favourite occupation is group sport. A few enjoy school work, but this interest is scarcely present in the seniors. Other categories show the unusual responses given almost equally by both groups.

The boys like to be with others of their own age and sex, and although some juniors (understandably) prefer a relative, this preference is characteristic of recidivists in both age-groups and was not stated by any first offender. In Raven's standardization none of the 12-year old boys made this reply, while in Foulds's comparison of the responses of normal boys and mentally defective delinquents, the latter's preference for a relative was significantly greater than the former's (Foulds, 1950). But ordinary boys generally have frequent access to their relatives, while Foulds's group "is now to be found in an institution which harbours mentally defective juvenile delinquents"; moreover, first offenders are not likely to spend long periods in Remand Homes and Approved Schools. There is thus a tendency for the delinquent character to associate to a relative, but a higher frequency of responses from first offenders and recidivists both living in an institution would be required to establish the connection.

When asked whom they disliked being with, subjects generally responded with the name of an existing playmate (of their district or in the Home); other subjects disliked a group, thus, "those that steal", "the rough boys", or "the boys that get you into trouble" were popular responses. While the apparent simplicity of these replies may be a product of the subject's attitude to the experimenter and an attempt to cut a righteous figure before him, the subject's eagerness to dissociate the boy from his morally inferior playmates becomes, as responses to the final question show, an assertion that the imaginary boy

differs from the subject by reason of the moral superiority of the latter. This item could profitably be amplified by adding "Why?" after the answers; the link between these subsequent responses and the replies at the end of the test where the subject's reasons for disliking the boy are stated would then show first, whether the moral attitude had been retained throughout the conversation, and secondly, by a comparison with the replies to Q.10(c), how characteristic of the subject the attitude was.

The boy shows his friend a secret (Q.4). To the juniors the secret is an object of potential and (to them) inestimable value, such as treasure, jewels, lead or money, but when replies are pursued (Q.4b), the boys would only play with it, have it stolen from them, or be reported to the authorities by their friend. Such responses were given by recidivists of both age-groups; it was given by only one first offender and by the four most persistent offenders of the sample, while the seniors' most popular response (animals, birds and nests) was given by first and occasional offenders of all ages. In Foulds's group of defective delinquents, the response "nests and birds" was given by only 2 per cent. as against 85 per cent. who responded with "real things" or "playthings", while for his normal boys the percentage for the "nests and birds" category was 39, and that for "real things" and "playthings" was 26. From Raven's sample "birds and nests" is the most popular response; it was given by 76 per cent. of his 12-year olds, and none of the remaining 24 per cent. gave a response involving playthings. The data from these three sources therefore suggest that responses involving material things to be played with are associated with younger boys and in particular younger delinquents.

The stories which the boy tells his friends (Q.6a) fall into fairly distinct classes when the subject matter forms the basis of classification rather than, as in Raven's and in Foulds's studies, the kind of narrative. These writers classed the stories as Boastful Stories, Imaginary Stories, Gossip, Expedient Lies, and Raven comments that "whichever way the responses to Q.6 were classified, the groups tended to merge the one into the other". Reference to the subject matter of these stories (in the Summary of Results above) shows that this is hardly surprising; most of the stories could be put into any of the groups; moreover, while the wording of the question makes its meaning clear to an adult, not all the delinquent subjects understand the same thing by "story". The new grouping adopted is according to subject matter, and this has the additional advantage of showing at a glance what kind of stories the boys tell, which is in keeping with the object of the test. Junior boys tend to tales of stealing, while in this and in Q.6c senior boys make up the difference with boastful stories unconnected with stealing. The boastful stories of the juniors mainly concern hidden treasure or variations on the "family romance" theme, while seniors boast of everyday events such as promotion in the school team. Tales of stealing are always purposeful: they imply a boast, a denial, or an accusation; subjects whose story is of stealing invariably make a reference to stealing in their replies to the final question, usually with an assertion that they differ from the imaginary boy in that they do not steal nor do they mix with those who do steal. Replies to Q.6b, "Was it true? Why did he tell them it?" which Raven hoped would elicit the motives for telling stories have not been classified because the reason given was merely that a story had been asked for; thus, "Because he wanted to" was the invariable reply.

The wish which subjects want to come true (Q.8c) is for playthings. The only important difference between juniors' and seniors' wishes is that whereas 5 seniors wish for the welfare of their family and no junior does, 5 more juniors

respond with a "magical" wish for treasure, gold, etc., similar to the secret which they showed their friend. Apart from these categories, the responses of delinquents follow closely the responses of Raven's normal 12-year old boys.

With the sum of money (Q.8d) both juniors and seniors would buy cars, cycles, sweets, etc., and "save the rest". They do not give many presents, as normal boys do, except for treating their friends to sweets or to the pictures. A type of response which does not occur in the normal sample is that under the heading "Reparation", so called because of the guilt motive and the intensity of feeling with which the response was made; this is the desire to give all the money to the parents, "every penny of it"; this category accounts for more than one-fifth of the responses, and not by any first offender.

The attitude to growing up (Q.9) is positive, and, as with normal boys, rather less than a quarter of the sample want to stay young. Four of the 9 first offenders want to stay young; the majority of subjects, including the 9 most persistent offenders, want to grow up to work.

2. *Parents* (Qs. 2a, 2b, 6c)

The boys visualize their parents' getting cross with them because of their disobedience; examples being running into busy streets, taking food from the larder, staying out late, etc. Such is also the disobedience of ordinary boys from whose responses both Raven and Foulds arrive at the same principal category. The second category includes those whose misbehaviour at home has an aggressive tinge, such as throwing stones, bullying, being rude, or defacing something. Although in Raven's and Foulds's studies there is insufficient detail to make a comparison, certain differences between normal boys and the Remand Home sample are apparent: (1) the delinquent boys are not scolded for being destructive; no responses classifiable as deliberate destruction were made, though 20 per cent. of Raven's 12-year olds and 12 per cent. of Foulds's normals were of this type. Parents of delinquent boys may not interdict this form of misbehaviour very strongly. (2) But 10 delinquents are punished for some event beyond their control. Of all the boy's recent memories of home, the parents' anger over an *accident* comes to mind; he anticipates punishment for a misfortune in which he is involved rather than for such misdemeanours as brought him to the Remand Home. (3) Only 8 delinquents suffer because they break the law. This response was made by only two juniors and six seniors, all frequent offenders. It is therefore not widely perceived as a motive for parents' anger. Since the proportion of juniors is so small, the sympathy felt for the detainee may have waned by the time he has become a recidivist senior.

The consequences of the parents' anger (Q.2b) fall mainly into three groups evenly represented by juniors and seniors: (1) Forgiveness, with or without an expiatory act. (2) A smacking or worse, particularly in the case of frequent offenders. (3) Mild, non-corporal punishment, particularly for first and occasional offenders. It is noteworthy that only 6 of the 86 boys visualize being "sent away", while Raven's largest category (36 per cent. of his 12-year olds) make a response classifiable as "banishment". Perhaps for the Remand Home boys the "banishment" has in some sense occurred and is therefore not feared so much.

The stories that boys tell their parents (Q.6c) fall into clearly demarcated groups when classified on the basis of subject matter. The emphases are on stealing and harm. An interesting contrast occurs in the stories boys tell their companions. Boastful stories drop to third place and no longer concern possession or ancestry, but achievement or promise; they are told not to arouse envy but to create pride or promise reparation. Subjects who in Q.6a sought to arouse

the envy of their companions, now want to make their parents proud of them. This applies particularly to the seniors, but if the 11 cases of the sub-grouping "he didn't do or wasn't going to do anything wrong" (which constitutes a kind of boast) are added in, the juniors' and seniors' responses distribute evenly, and replies concerned with evoking the parents' pride in their boy will be numerically the largest category. It is evident that these delinquent boys are much troubled about their parents' good opinion of them, while the answers to Q.6a show that they are also concerned with the approval of their fellows and how they try to obtain it. Boastfulness is only one way of drawing attention to oneself, and the desire for the parents to notice and interest themselves in their child is subtly expressed here. The responses mainly derive from a desire to be wanted, to be protected or to be punished. Responses involving wrongs, harm and running away, which occupy such a small place in the stories the boys tell their fellows, become the most frequently told stories to those whose duty it is to want, protect, or punish them.

3. *Hopes, Fears, Dreams* (Qs. 7a, 7b, 8a, 8b, 5)

When the boy goes to bed (Q.7a) he tends to think about what he will do the next day in school or at play, or to phantasy on his working as a grown man. The responses in this category have no unpleasant flavour; they are concerned with boyish aspirations or future pleasures evoked by pleasant memories or sport, the school, the cinema, and friends. Some juniors think about their parents, which is to be expected from youngsters in an institution. It was necessary to make two categories of responses occasioned by guilt and fear, which previous investigators classed as "difficulties". It is important to know what these difficulties are, whether they concern the consequences of past crimes, anxiety for the future, or the numerous trivial mistakes indicative of a persisting guilt which keeps the boy ever remorseful and defensive. Instances of the latter are provided by the 8 subjects who were remorseful over nothing in particular. Only 4 subjects mention theft, which is the principal cause of all the subjects' remand. In the larger categories, juniors and seniors are fairly evenly represented, and no type of response is related to recidivism.

The boy cries (Q.7b) chiefly because of an injury which he suffers by accident ("he fell and cut himself") or by someone's intention ("his father hit him"). This is also the principal category in Raven's and in Foulds's results. "Fearful thoughts", however, under which could be grouped at least half the responses of all juniors and seniors, are given by only 8 per cent. of Raven's 12-year olds, and by more of Foulds's delinquents than his normals. Various configurations of guilt, aggression and fear account for the remaining responses, and it is difficult with the present data to determine a suitable principle for classifying them. More suitable categories may emerge when larger groups are compared; it is sufficient to note at present that juniors and seniors are about equally represented in the large categories, and that the "fear" response is characteristic of the delinquent sample.

When he falls asleep (Q.8a) he dreams of events which (with a few exceptions) can firstly be classed as "pleasant" or "unpleasant", and secondly according to content. Of Raven's 12-year olds nearly half have nice dreams, while the other half dream of worries or catastrophes. "Nice" dreams account for over half of both Foulds's groups. It is worth finding out what constitutes a "pleasant" dream. For the Remand Home sample it consists in being given a present, being in an exciting situation, being promoted in one's group, or in doing man's work well—in short, in getting something, or in being something

different. In the second category, dreams with an unpleasant flavour have been subdivided into aggression towards or punishment of himself, guilt for past and contemplated misdeeds, and aggression to others. Juniors preponderate in the number of unpleasant dreams, but not significantly so, and in the next question the seniors' deficiency is made up.

What makes the boy wake in the night? (Q.8b). In this question guilty and frightening dreams are the chief category. This item provides a better opportunity for projection. In the previous question the boy is asked for a dream and he replies with a story, while here the cause of a disturbance is asked for and a dream is supplied. These dreams are therefore less forced, and it is highly suggestive that they all involve guilt or fear, which those supplied to the previous question do not. Thus in the last question there are dreams about "getting a new bicycle", while in replies to this question all dreams have a moral or punitive flavour, most are nightmares, and only three are about love-objects. Comparison with responses in the two previous studies is not possible, for they both have "Disturbances" as the chief cause of the boy's awakening in the night, which seems to beg the question. In the Remand Home sample, then, the cause of waking in the night is, for 60 out of 86 boys, a cause involving fear; seniors preponderate in category A, juniors in category B, but the result is the same: a fear response is made by 31 juniors and 29 seniors.

What gave the boy a fright? (Q.5). Nearly all subjects reply, "He got scared". This is the most frequent reply of Raven's normal boys and of Foulds's two groups, so in both these studies "Being scared" is the principal category. But this answer merely restates the question; the delinquent boys' replies were pursued until some cause of being scared was given. The favourite themes then re-emerged, with both age groups evenly represented in each category. Responses concerned with bodily harm to the self or others (59); stealing (18); losing something (5); and the frightening (5).

4. *Projection*

"*That's the end. What do you like about the boy in the story?*" (Q.10a). In this and the remaining two questions the subject discusses with the experimenter the story he has just told. The observable reaction on learning that the story is over is the relief of the subject and his eagerness to depart. The subject has vested the boy in the story with certain qualities and attributes, and now has an opportunity of giving his opinion of them. He will be expected to like the imaginary boy for his good qualities, and replies to this question will show the sort of qualities which the subject holds to be of value. The question met with so much resistance or lack of understanding that the interrogation had to be pursued indirectly; first, by asking, "Do you like the boy in the story?" and then introducing the test question only when subjects had had time to formulate their ideas.

Responses were first grouped according to whether subjects liked or disliked the imaginary boy, and secondly according to the reasons given. On this basis, the imaginary boy is chiefly liked, and liked for a negative reason: because he is sorry for his lies, thefts, truancies, or because he promises not to be naughty again. In the second category he is disliked for much the same misdeeds; when these subjects were pressed, "You surely find something to like in him?", they could still persist in their total dislike. Neither of these two categories, in which juniors and seniors are almost equally represented, would apply to the responses of Raven's ordinary children, all of whom liked their "hero", and liked him for such positive qualities as appear in the responses of subjects in

category C, or for other reasons. Similarly with Foulds's two samples: all subjects have some reason for liking their hero, either because of his virtues or because nice things happen to him. The strong guilt motive appears to be peculiar to the Remand Home sample. The severity of subjects' judgments on their creation is a tribute to the frankness with which they have spoken their thoughts and an indication of their moral attitude towards the behaviour which they have described. Aside from the fact that subjects have openly and covertly drawn on their own experiences in telling the story, the extent to which the story constitutes a valid projection record can partially be assessed by responses to this question. Of the 73 subjects who understood the question, none of whom is a first offender, 51 have ascribed to the imaginary boy thoughts and behaviour which they disapprove of, except the thought of his being sorry for that behaviour. Of these 51 subjects, 33 like the boy because in reply to previous test questions he had been sorry for his misdeeds or had tried to make amends. A further 17 subjects, in whose story the boy is characterized by acts of kindness, generosity, sportsmanship, etc., rather than by villainy, state that they like the boy for such acts. Two subjects like the boy because he told lies and "got away with it". One subject says he has been describing himself. In respect of these qualities of experience the subjects have attributed their own thoughts and feelings to the boy in the story.

Of all the test items, this was the most difficult one to get over to subjects. A classification of first replies would not have yielded projection responses. Thus, "I like the boy—because of everything" was not accepted, nor was an answer based on an event described by the test question, such as, "Because he got £1,000" though both Raven and Foulds recorded and classified this kind of answer. The writer pursued the response until the subject gave a reply that was both meaningful and original in the sense that it was not contained in the wording of a test question. If no such response could be elicited the reply was labelled "Question not understood".

Failure to grasp the meaning of this simple question raises a new problem. The writer has noticed, in talks with the boys under different circumstances, that some boys "like" only persons who give them things and not persons whose company they enjoy. When they say that they like their mother or a companion, they spontaneously qualify the utterance with a short inventory of the things she gives them. Their friends, i.e. those whom they play with, do not give them things. Thus they make a distinction between those whom they like on the one hand, and their friends on the other. In the next test item the subject is asked what he dislikes about the boy, and only 4 subjects fail to understand the question. Now if the subject receives things only from a few close relatives, the concept of "dislike" would be more applicable to the imaginary boy than the concept of "like", and a smaller number would fail to understand it. In fact, for those who had difficulty in answering this question, "like" and "dislike" were not contradictories; they merely applied to different fields of interest. Failure to understand Q.10a occurs in both normally and subnormally intelligent subjects, but twice as often in the juniors.

"*What do you dislike about him?*" (Q.10b). Responses under the heading "Tells lies" were grouped apart from "normal faults" partly because of the high incidence of the former and partly because the method of testing may have produced this result. The subjects have been telling a story; they knew that they could answer as they wished. But it emerged that for some subjects there is little or no difference between a story, a joke, a tale and a lie. Thus in Q.6b, where a story is asked for, 16 subjects (8 juniors and 8 seniors) interpret "story"

as "lie" or believe that a lie is being asked for. When Q.10b is presented these same 16 subjects dislike the imaginary boy "because of those lies he told the others". An inability to make distinctions in kinds of narrative is not so characteristic of these subjects as is a confusion in their understanding of the moral issue of the untruth. Even if the subject did understand that a narrative need not be an untruth, particularly when told to the investigator in a testing situation, he might still have intended to tell a lie in his story to the other boys. If so, the "tells lies" response will not have been produced by the method of testing but will be a genuine reason for disliking the imaginary boy. In future testing, first replies to this question should be pursued until a concrete example of the fault causing the dislike is offered. This example can be recorded and compared with the faults attributed to the boy in answers to earlier questions. The superiority of seniors in the principal category and of juniors in category C (subjects who dislike nothing about the boy) may be the result of the upsetting influence of the "lies" response. The question produced almost equally balanced numbers of responses in the other categories. Comparison with other samples is not possible, for most of Raven's group have a "nothing" response, as do Foulds's normal group, while 44 per cent. of his delinquents reply, "He was naughty" without specifying what the naughtiness consisted of.

"*Is he the same as you? In what way? (Or, in what way isn't he?)*" (Q.10c). In the final question the subject is invited to compare himself with the imaginary boy he has described. Responses were first classified on the basis of the subject's initial statement, i.e. as to whether he admitted or denied resembling the boy. Of 83 subjects, 53 gave a negative response; when the question was pursued, however, these subjects could find few points of difference. Most subjects stated that they did not steal, lie, or behave so badly as the imaginary boy. This result has something in common with the finding of Jackson from projection responses to a series of drawings designed to elicit children's attitudes to aspects of family life (Jackson, 1950). Of three pictures, the types of responses to which showed significant differences between the normal and delinquent groups (but not between the normal and neurotic), the child was perceived as being "naughty" or "bad" more frequently by the delinquents, a *light* punishment was imagined more frequently by the normals, and the child as playing or being industrious less frequently by the delinquents. "The examination of these data shows that the delinquents exhibit a pronounced trend towards 'bad identification', or, if the child in the picture stands for a sibling or play companion, they project their own feelings of badness on to him" (Jackson, op. cit.). The Remand Home boys, category A, emphasize that they are not the same as the boy they have described, and the differences given are moral; in other respects they are the same.

In the third category, 18 subjects also deny their resemblance to the boy, but when points of difference are asked for, small details of clothing or place of residence are given, or the difference is in an event suggested by a test question, and when pressed, they can find no other difference. It is important to note, particularly for this category, that subjects were given ample time and encouragement to state how they resembled and differed from the boy; when asked, the investigator recapitulated the substance of the subject's story.

If, to the 2 responses in category F (in which the subject says he has been describing himself) are added the responses of category B (in which the subject admits his likeness or complete similarity to the boy), and the responses of category C (in which similarity in insignificant details only is denied), a total of 48 out of 83 boys can be classed as admitting directly or indirectly to having ascribed their own phantasies to the imaginary boy.

Only 5 subjects give themselves a position morally inferior to that of their creation, and this is in each case a matter of small degree; the subject is similar to the boy except that he is a little less kind or honest, or does not get into trouble so much. None of these 5 subjects is a first offender, and 2 are of the most persistent offenders' group. Age seems to have a bearing on this kind of response, but as only 5 out of 83 are involved, numbers would have to be augmented to assess its significance for age statistically. The importance of the response lies in its relation to recidivism.

V. Conclusions

The summary of answers to test questions indicates the kinds of responses elicited by the Controlled Projection Test and their incidence in a sample of juvenile delinquents. All subjects took the test very seriously and "felt themselves" into the standard situations. They drew extensively on their own feelings and experiences for their answers, and at the outset identified with the boy in the story, vesting him with the moral standards they esteem and attributing to him the behaviour they denounce. From the most frequently occurring responses a composite version of the group's stories can be drawn up:

> The boy is between 8 and 17 years old, enjoys games and sports with others of his age, and has little interest in schoolwork, especially if he is a senior. He is quick to dissociate himself from "those that steal". At home his parents get cross with him when he is disobedient or disagreeable, whereupon he will more often be punished than not, usually with a smacking or worse. He is perceived as an object for his parents' aggression when domestic upsets occur, and is himself generally the cause of their quarrelling; in both cases the boy suffers. He likes to think of having a pet animal or secret hideout; if a junior he prefers to imagine that he has hidden away jewels or money which will in due course be stolen from him. He is easily frightened by visions of falling and cutting himself or breaking a limb. He arouses the envy of his friends with boastful stories of a possession, of stealing, or of noble ancestry, but the stories to his parents imply his exaggerated need of their approval and protection. In bed he thinks of his future pleasures and prowess, and to a lesser extent of his misconduct. Phantasies of getting hurt or being assaulted could make him cry, as would remorse over his misdeeds or their consequences. When asleep he tends to have nightmares, particularly if he is a junior; to a lesser extent he dreams of pleasant events. Whatever his age, night disturbances are caused by frightening dreams or noises provoking fear. His greatest wish is for a plaything such as a bicycle, and if given a large sum of money he would spend it thus, perhaps saving a little. He emphatically dislikes a boy who behaves as he does, except in so far as he is repentant.

While the group responses show the kind of phantasies nurtured by the subjects, reference can be made to individual records to study the configuration of thoughts operating in a single subject. Whichever way test replies are studied, the projection records for juvenile delinquents give a picture of a boy inevitably getting into trouble, fearing the expected punishment, over-eager to make amends, and preparing for the next repetition of this cycle.

The importance of the material elicited justifies the carrying out of further studies in Controlled Projection using larger numbers of subjects and in different clinical fields.

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A RATING SCALE DEVELOPED FOR USE IN CLINICAL PSYCHIATRIC INVESTIGATIONS*

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Introduction

The impulse to attempt this study arose from difficulties encountered in the process of trying to demonstrate the efficacy or inadequacy of various methods of psychiatric treatment (Monro, 1950; and Monro and Conitzer, 1950). The problem which arose was that of matching groups, whose composition necessitated a struggle with diagnostic and prognostic criteria difficult to define and still more difficult to secure agreement about. The chief trouble derived from the fact that the systems of classification in normal psychiatric use had their roots in the past, when the cases were dealt with at a more advanced stage, or were of a more serious nature, than many which are today seen in out-patient clinics and mental hospitals. In the search for a more adequate system of classifying recent and therapeutically promising cases, the work of Cattell (1946) suggested a possible method of advance. It seemed sound to hope that the application of modern psychological techniques to psychiatric problems would be as useful as past applications of the principles of physiology and pathology to clinical medicine.

The following quotation from Sargant and Slater (1950) showed that others were in the same difficulty as myself: "In psychiatry today we have reached a curious state of affairs in which we are aware of the value of a number of treatments but do not understand their indications. We can, indeed, get a considerable amount of guidance from established systems of diagnosis and classification. The schizophrenic pattern, for instance, cannot be treated on exactly the same principles as the neurotic. But the indications provided in this way are not by themselves sufficient, and are actually neglected by some clinicians. We should be able to add to them more refined methods of assessing therapeutic needs. This is, unfortunately, not common practice; and what we see instead is the application of rule of thumb and personal bias."

The work described here is an attempt to advance towards greater precision and sophistication in recording psychiatric data, as a necessary preliminary to a more exact use of treatment methods.

Brief Historical Survey

The number of correlation studies and factor analyses in the psychiatric field is small. Those which are most important in demonstrating the historical setting of this study are: Moore (1929), Eysenck (1944), Cattell (1946a), Burt 1947-8), Wittman, Sheldon and Katz (1948), Linford Rees (1949, 1950), Loor, Wittman and Schanberger (1951).

* This article is an abstract of part of a thesis accepted for the degree of Ph.D. in the Faculty of Science of Edinburgh University.

The principal sources drawn on in relation to factor analytic study were: Thurstone (1935, 1944), Burt (1940), and Holzinger and Harman (1941).

The principal works drawn on in relation to the study of personality were: Allport (1937) and Cattell (1946). The reasons for giving considerable weight to the work of Cattell as a starting point were as follows. Cattell has worked in the clinical field as a psychologist; he is therefore clinically oriented and shows more appreciation of the problems of the clinician than some other research workers. He realizes the value of the clinical tradition, while making concrete suggestions about refining clinical methods. Lastly, his concept of the personality Sphere and his Comprehensive Trait List are important technical tools in maintaining a "molar" rather than a "molecular" approach to the study of personality.

Plan of Present Enquiry

It is generally agreed that it is impossible to describe personality intelligibly without using trait terms. The manner of using them, is, however, important. Cattell (1946, p. 59) says: "Clinical psychology has always taken traits—as descriptive elements—for granted, turning its interests to the syndromes that may be made out of their patterning. When one comes to the end of the clinical approach, however, and begins to follow the penetrations which modern psychological method has made into the subject of personality description and measurement, he is forced at once to take a more sophisticated view about the nature of traits, to enter upon an entirely new vista of concepts and a new discipline of thought."

For the purpose of this enquiry, the definition of a trait given by Cattell (1946, p. 61) has been accepted: "A trait, whether unique or common, is a collection of reactions or responses bound by some kind of unity which permits the responses to be gathered under one term and treated in the same fashion for most purposes." This does not differ substantially from Eysenck's (1947, p. 28) definition of traits as "Observed constellations of individual action tendencies." Furthermore, Cattell's contention (1946, p. 71) that covariation is the basis of functional unity was accepted as a working hypothesis. So, broadly, were Cattell's suggestions as to the difference between source and surface traits (1946, p. 78), and his scheme (1946, p. 131) of the hierarchy of trait, type, factor, cluster, syndrome and trait element.

Having clarified the manner in which the word "trait" was to be used, the next step was to select the method of personality exploration. Of the three principal methods, the use of questionnaires was rejected as quite unreliable in relation to mentally disordered patients. Objective tests were also discarded as being available only for a very restricted part of the whole field of personality. Rating was left as the method of choice. The possibility of using projective tests and case studies was considered but rejected owing to the likelihood of subjective bias and the difficulty in quantifying results. Rating, moreover, has certain positive advantages. It is the only method which can deal with a sufficiently wide variety of personality elements at one time, to enable one's approach to be molar, not molecular. Also, of the three methods, it is the most closely related to real life situations, in which the clinician is primarily interested. Lastly, as Cattell (1946, p. 212) has pointed out, it is the best method for providing perspective, the scaffolding within which accurate objective tests can be worked out. Rating, if carried out with proper safeguard, can rival objective tests in accuracy (Cattell, 1946, p. 213). This point is taken up later in regard to this enquiry.

Having chosen the rating of traits as the method of enquiry, the next step was to select a list of traits to use. Cattell's list (1946, p. 219) was chosen for the following reasons:

1. It is a comprehensive instrument for the description of personality, being derived from the Odbert-Allport trait list by the cancellation of synonyms and the addition of technical psychological terms for which a colloquial English word would not be suitable.

2. Most psychiatric rating scales, e.g. that of Malamud and Sands (1947) throw into relief the characteristic behaviour of mental hospital patients, while paying too little attention to the gradations of behaviour in which the psychiatrist is not immediately interested. This introduces an unknown degree of bias into a comprehensive investigation of personality.

3. By using Cattell's list, his work with it on normal populations was made available for purposes of control.

4. This list appeared to be the best available compromise between comprehensiveness and compactness.

5. It was clearly better to use an established list than to try and make a new one.

6. There is already a more extensive literature of correlation clusters derived from the use of this list than from any other.

7. Cattell's concept of the Personality Sphere has won considerable recognition and forms a sound basis for further work. This concept is almost inseparably bound up with the use of a comprehensive trait list.

Alphabetical List of Traits

Absent-minded	Conceited	Extrapunitive
Accessible	Confused	Faddy
Acquisitive	Conscienceless	Fair-minded
Adaptable	Conscientious	Fastidious
Affected	Contented	Fickle
Affectionate	Conventional	Flattering
Agoraphobic	Co-operative	Forgetful
Alcoholic	Courageous	Formal
Alert	Cowardly	Forward-looking
Ambitious	Cruel	Frank
Amorous	Curious	Friendly
Apollonian	Cynical	Frigid
Argumentative	Deceitful	Frivolous
Arrogant	Decisive	Generous
Ascetic	Defensive	Genial
Assertive	Deliberate	Gentle-tempered
Austere	Dependent	Gloomy
Autocratic	Dishonest	Gluttonous
Awkward	Disloyal	Good-tempered
Banal	Disordered in thought	Grateful
Boastful	Dissatisfied	Gregarious
Brooding	Eager for attention	Habit-bound
Careless with goods	Easy-going	Hard
Casual	Eccentric	Hard-headed
Cautious	Egotistical	Headstrong
Charming	Emotionally Expressive	Hearty
Cheerful	Energetic	Honest
Claustrophobic	Enterprising	Hostile
Clear-thinking	Enthusiastic	Humanitarian
Coarse	Erotic	Humble
Cold	Evasive	Humourless
Cold-hearted	Excitable	Hurried

Hypochondriacal
Idealistic
Imaginative
Imitative
Impatient
Impulsive
Inactive
Independent
Individualistic
Inflexible
Inhibited
Interests Narrow
Interests Wide
Introspective
Intrusive
Intuitive
Irresponsible
Irritable
Jealous
Kind
Labile
Lax
Leading
Leisurely
Listless
Logical
Loyal
Masochistic
Memory Good
Mirthful
Mirthless
Mischievous
Modest
Mulish
Mystical
Naive
Natural
Neurotic
Obstructive
Opinionated
Optimistic
Original
Painstaking
Partial
Patient
Peaceable
Pedantic
Pernickety
Persevering
Pessimistic
Phantasying
Phlegmatic
Pious
Placid
Plaintive
Planful
Planless
Poised
Polished
Praiseful
Psychotic
Pugnacious
Quiet
Quitting
Reasonable
Rebellious
Reckless
Reliable
Reserved
Responsible
Retrovert
Reverent
Rough
Ruthless
Sarcastic
Secretive
Self-confident
Self-controlled
Self-deceiving
Self-denying
Self-dissatisfied
Self-distrusting
Self-effacing
Self-pitying
Self-respecting
Self-sufficient
Selfish
Sensitive
Sensual
Sentimental
Serious-minded
Settling Down
Shiftless
Shrewd
Shy
Slanderous
Sleeps Poorly
Sleeps Well
Slipshod
Sociable
Soft-hearted
Submissive
Suggestible
Suspicious
Taciturn
Tactful
Tactless
Talkative
Thoughtful
Thrifty
Tight-fisted
Tolerant
Tough
Trustful
Unambitious
Undependable
Unenquiring
Ungrateful
Unimaginative
Unrepining
Unresentful
Vacillating
Versatile
Vindictive
Vivacious
Wandering
Witty
Worldly
Worrying

Abilities

Drawing
Mathematical
Manual Dexterity
Mechanical Aptitude
Musical Aptitude
Physical Strength
Spatial Ability
Verbal Aptitude
Intelligent
Unintelligent

Special Interests

Aesthetic
Artistic
Economic
Home and Family
Music
Physical Activity
Political
Religious
Social
Theoretical
Technical

Having selected the method and the trait list, the remaining steps to be taken became clear, as follows:

1. The denotation or "operational definition" of each trait in terms of actual behaviour.
2. The selection of the sample population to be rated.

3. The rating of a number of cases in conjunction with colleagues, to test the accuracy of the method and to estimate the degree of personal bias on my part.

4. The actual rating of the experimental population.

5. The mathematical computation of the results.

The Denotation of Trait Terms

Before this work was begun, the decision was reached to use tetrachoric correlations in computing the results. The argument against tetrachorics was that their use might result in a degree of crudeness and artificiality. Against product-moment correlations however, the arguments were decisive. Apart from the appalling mathematical labour, there was the difficulty in arranging the steps in a rating scale without being grossly arbitrary. In addition, if such a scale were to be constructed, there was the probability that the middle ranges would be mainly used. The decision to use tetrachorics made the task of providing operational definitions much easier, as it was only necessary to describe the conditions from which the presence of a trait could be inferred, or, in other words to define the circumstances which justified a positive rating.

The task of furnishing the operational definitions was undertaken by a committee of six, including Professor A. R. Humphreys of the Department of English, University College, Leicester, Mr. A. G. Crammer, late Headmaster of the City Boys' School, Leicester and myself. Much valuable help was given by the Philosophical Section of the Leicester Literary and Philosophical Society, under the Presidency of Dr. P. M. Leon of University College.

In framing the definitions, the following principles were adopted:

1. The opposite poles of Cattell's bipolar traits were separated, and each term dealt with as a trait in its own right.

2. It was agreed to be impossible to provide an exhaustive list of the actions which could be taken as grounds for a positive rating of any particular term. Pushed to extremes, such a course would have required, in regard to the term "Hostile", including in the definition the giving of a left black eye and the giving of a right black eye. In other words, it was found to be impossible to construct a behaviour sphere to correspond to Cattell's "Personality Sphere". The definitions were therefore framed in terms of broad classes or types of behaviour, rather than in terms of detailed actions.

3. The part played by empathy or insight in arriving at a rating was felt to present considerable difficulty. This, however, was considered to be met in practice by the technique of rating in conjunction with colleagues and demonstrating a measurable degree of correlation.

4. Where two terms in Cattell's list were found to have virtually identical operational definitions, one was eliminated as redundant.

5. Where a term was found to be vague in meaning, it was also eliminated.

6. Some of Cattell's words, especially neologisms, were changed for others in more common usage.

7. Psychological terms derived from research were only retained if an adequate alternative could not be found.

All the workers on this task were surprised at the degree of agreement reached and the ease with which it was achieved.

After discussion and work lasting nearly a year, 45 terms were rejected as redundant or vague, and 7 terms were added, leaving a total of 246 provided with operational definitions. Of these 24 were changed in name, though retaining substantially the same meaning.

Lastly, it was decided not to mix the results of rating with those from objective tests except in the case of intelligence, where it was felt to be pedantic to ignore testing in favour of some newly evolved ad hoc criteria.

The full list of trait terms and definitions covers some fifty pages of typescript. In this paper I must therefore be content with giving a small sample of the definitions to show the kind of criteria evolved, followed by an alphabetical list of the traits included.

Sample Definitions

ALERT. Rate positively those who show the capacity for observant concentration on their surroundings and the power of rapid appropriate action in regard to them, whether at work, at play or in social relationships.

BROODING. Rate positively one who ruminates on painful topics or emotional hurts to a degree which is observed by others or felt by the subject to reduce his efficiency at work or to make him curtail or refrain from spare-time activities of an active or constructive kind.

CAUTIOUS. Rate positively one who observes and attends closely to situations in which he is involved, and uses forethought to order his actions in such a way as to avoid unpleasant repercussions.

DISSATISFIED. Rate positively a person who frequently complains about his lot; who feels deprived of something to which he is entitled; who feels that he has a grievance against life; who is eager to change his position and circumstances although there are no good reasons for so doing.

EXTRAPUNITIVE. Rate positively a person who does not admit to being in the wrong in the absence of conclusive proof, and even then struggles to the last against the admission: one who lays the blame on others for his own actions or their results; one who is demonstrably more critical and fault-finding towards others than towards himself.

FRIVOLOUS. Rate positively a person who frequently or habitually attempts to make light of matters which ought to be taken seriously.

GREGARIOUS. Rate positively a person who feels the need of company and dislikes being alone, but who does not necessarily show any distinct social expertise.

HOSTILE. Rate positively one who frequently picks quarrels; who has few friends but many enemies; whose spontaneous attitude to others is one of dislike which has to be overcome.

IRRITABLE. Rate positively one who frequently loses his temper over trifles.

LAX. Rate positively one who transgresses the moral code accepted by his fellows, e.g. in business or professional conduct, or in the sexual or social sphere, because he himself accepts a lower standard as adequate or advantageous.

MISCHIEVOUS. Rate positively one who thinks it funny to cause other people minor hurts or annoyances.

PEACEABLE. Rate positively one who is only with great difficulty provoked to quarrel, who dislikes fighting and always prefers a peaceful settlement of a difference if possible.

CHOOSING THE SAMPLE POPULATION

In this task it was accepted that:

1. All well-known personality types and clinical syndromes must, if possible, be included.

2. The sample must be as nearly as possible representative of the mentally disordered population of the country.

Random sampling was rejected, as rare types or clinical syndromes might be excluded quite fortuitously. Clinical classification was relied on as the guide to sampling. As regards size, a population of 200 was chosen as being large enough to yield useful information, while small enough to allow of careful individual study of each patient.

Carlton Hayes Hospital, near Leicester, where this part of the enquiry was undertaken, provided a remarkable cross-section of the country as a whole. The catchment area included city suburbs, small industrial towns and villages, an area of mining and heavy industry and a large rural population. The hospital has a substantial number of amenity beds, so all income groups except the highest were included in the sample. Further, virtually all the psychiatric service for the area, with the exception of that for the wealthy, was provided by the hospital and clinics under its auspices. A very comprehensive view could therefore be taken.

The selection of the sample was a matter of extreme difficulty in view of the absence of recent or reliable figures of the incidence of the various forms of mental disorder. All cases with a discoverable organic component were excluded. Also, only in-patients were rated, with the exception of a small number who ought to have come into hospital, but refused, about whom exceptionally good information was available.

The age distribution of the sample was as follows:

Under 20	12	30–34	39	45–49	20
20–24	22	35–39	23	50–59	17
25–29	39	40–44	24	60 or over	4

Men and women were selected in the ratio of 3 to 4, in accordance with the figures given in the report of the Board of Control (1950). This ratio also obtained in the ratio of male to female admissions at Carlton Hayes Hospital. The actual numbers chosen were 86 men and 114 women.

As has already been said, it was very difficult to decide how many cases from each clinical category to include. A sample regarded as the best possible in the circumstances was chosen after consulting the following sources of information:

1. A letter from the Board of Control giving the figures for admissions in each clinical category in England and Wales during 1937.
2. The figures quoted by Cattell (1946) for first admissions to American State Hospitals, classified according to diagnosis, for 1936.
3. The "Statistical Abstracts for the U.S." (1949) which gave the same information for the years 1945 and 1946.
4. A careful study of the diagnostic trends, and changes in the type of admission to Carlton Hayes Hospital during the years 1935 to 1950.

The constitution of the chosen sample is set out in the table below; the classification of the less well-defined categories of disorder was determined as follows:

1. Those classed as "Anxiety States" were those patients placed in Category 310 of the 1948 International Classification.
2. Similarly those classed as "Hysteria" came within Category 311 of the same classification.
3. Obsessional states were in Category 313.
4. Neurotic Depressions were in Category 314.
5. The designation "Miscellaneous" included all cases in categories 312 or 315 to 323 inclusive.

Table showing composition of the sample rated

	Women	Men	Total
Schizophrenia	9	10	19
Manic-Depressive	21	17	38
Paranoid	3	3	6
Involutional	3	1	4
Schizo-Affective	7	5	12
Anxiety States	18	13	31
Hysteria	18	13	31
Neurotic Depression	15	10	25
Obsessionals	3	2	5
Miscellaneous	17	12	29
	114	86	200

The Rating of Cases in Conjunction with Colleagues

Two colleagues, a psychiatrist (D.A.S.), and a psychologist (G.C.P.) collaborated with me in this work. A considerable difficulty arose from the fact that information about the patients was collected from many sources, including relatives, family doctors, parish priests, probation officers and welfare workers. It was clearly impossible for three investigators to interview these people, asking them the same questions. Accordingly, I prepared detailed case histories of 15 patients rated. These were about 5,000 words in length and were available to the three of us. If either of my colleagues wished more detailed information on any point of fact, he was free to ask me to get that information, and add it to the case history. My colleagues were free to see the patients as they wished, and were free to rate on the basis of their own observations or on the facts recorded in the case history, just as they wished. Two trial ratings in collaboration were first carried out with full subsequent discussion, to see whether there were any ambiguities in the operational definitions. The remaining ratings were then carried out without any discussion between us. One point remained to be cleared up. It was possible that the taking of the history by only one of us introduced a bias towards agreement that would not have been present if complete independence of investigation had been possible. We therefore rated four colleagues, well-known to us all. It was clear that our information was less complete about them than about the patients, but we believed that our "Areas of Ignorance" about our colleagues would coincide.

The correlations obtained between us were as follows:

		Patients	Colleagues	Combined
A.B.M. and D.A.S.	r=	0·82	0·92	0·83
A.B.M. and G.C.P.	r=	0·86	0·93	0·87
G.C.P. and D.A.S.	r=	0·84	0·91	0·84

The higher correlations obtained when rating colleagues disposed of the possibility that the case-history method had introduced a bias towards a spurious agreement. Experience gained in using this rating scale, since the completion of this study, suggests that it increased the measure of disagreement. Some recent ratings carried out in conjunction with medical colleagues have shown a correlation between us of plus 0·90 or slightly higher. The findings recorded in this section of this paper bear out the contention of Cattell (1946) that rating is capable of accuracy comparable to that furnished by objective tests by showing correlations between different observers of the order of plus 0·90.

Rating the Sample

Although the actual work of rating 200 patients was very laborious, there is fortunately no need to describe the process at length. Only two points need

to be stressed. Each patient was rated at the height of his disturbance. Also, a trait clearly shown to be present in the previous personality was rated positive unless there was evidence to show that it had disappeared in the course of the illness.

Computation of Results

In an R technique study with 246 variables, the number of correlation coefficients to be dealt with is 30,012. To have worked all these out would have been an enormous labour. An expeditious yet accurate technique had therefore to be devised whereby those correlations below the chosen level of significance could be eliminated without being worked out in full. By using a Powers-Samas accounting machine and Thurstone's Diagrams for computing the Tetrachoric Correlation Coefficient (Chesire, Saffir and Thurstone, 1933), a technique was evolved which, although still laborious, was just within the bounds of possibility. The steps taken were as follows:

1. Using the Powers-Samas accounting equipment, the number of positive ratings common to each trait and every other trait in the list was prepared. From these data the fourfold tables necessary for computing the tetrachoric correlation coefficients were prepared.

2. Each trait was given a code-number, and the fourfold tables for each trait in relation to every other trait were entered on stencilled sheets.

3. Working in reverse from Thurstone's diagrams, a set of tables was prepared, giving the figures which must be present in the first and third columns of the fourfold table for a correlation of 0·50 or more to be present. Two sets of tables were required, one for positive and one for negative correlations.

4. By using these tables, the correlations of 0·50 or more were picked out from each stencilled sheet by a reasonably rapid process of inspection.

5. These relevant correlations were worked out to 2 places of decimals by using Thurstone's Diagrams. The remainder were not computed.

The total number of positive correlations of 0·50 or more was found to be 2,588; the number of similar negative ones was 2,650. Later it was found possible to adopt a positive intercorrelation of 0·55 or more as the standard for the admission of a trait to a group, or correlation cluster. The number of such positive correlations was 2,039; the equivalent figure for negative correlations was 2,088.

The positive correlations between 0·50 and 0·54 were only used as confirmatory evidence where there was some doubt to which group a given trait should be allocated.

I should like to stress that during the whole process of computation and arriving at the groups formed by the various traits by virtue of their correlations, the traits were represented solely by their code numbers. The groups were derived on purely statistical grounds, without even an unconscious bias in favour of placing a trait in a group to which it appeared to belong on psychological grounds.

Derivation of Trait Groups (Correlation Clusters) from the Data

The method employed was as follows:

1. A card index was prepared with a card for each trait. On one side all the positive correlations with other traits of 0·55 or more were entered; on the other side the negative correlations of similar magnitude were recorded.

2. As the starting point for the formation of a group, a high correlation (positive) was selected. From the card index, it was easy to pick out a third trait with high correlations to both traits involved in the first correlation. This process was continued until the correlations "petered out", when a fresh start was made from another high correlation.

3. A graphic table of correlations was prepared in the usual way; the order of entering the traits on the graph was determined by the relationships revealed by the above process of sorting the cards.

4. Inspection of the graph showed that there were 30 rough groups, and some traits were clearly misplaced.

5. The next stage was a process of "Tidying up". Traits were placed in a group according to two principles:

(*a*) The number of positive correlations of the required magnitude with other traits in the group.

(*b*) The magnitude of those correlations.

As a rule, the second principle was used to arbitrate between traits with an equal numerical representation in two groups.

6. The majority of traits presented little difficulty, as their affinities were clearly shown by the correlations. When, however, misplaced traits had been correctly assigned, and all doubtful ones allocated, the number of groups had grown to 35, as set out below.

List of the 35 Groups obtained from the Data

The number on the right of the trait gives the weighted score for that trait within the group, as described below.

Group 1

Conscientious	10
Responsible	9
Painstaking	9
Reliable	9
Persevering	9
Self-respecting	10
Cautious	7
Serious-minded	9
Deliberate	7
Formal	7
Fair-minded	7
Thrifty	7

Group 2

Patient	15
Loyal	16
Honest	14
Self-denying	15
Kind	15
Soft-hearted	14
Unresentful	11

Group 3

Co-operative	12
Reasonable	11
Grateful	12
Natural	11
Tactful	11
Praiseful	10
Affectionate	11
Friendly	11
Frank	11

Group 4

Hearty	9
Optimistic	9
Cheerful	8
Genial	9
Self-confident	8
Vivacious	8
Mirthful	8
Unrepining	7
Enthusiastic	8
Charming	7
Energetic	7
Contented	6
Generous	6

Group 5

Adaptable	27
Gregarious	25
Curious	24
Frivolous	24

Group 6

Talkative	21
Boastful	21
Intrusive	21
Hurried	19
Emotionally expressive	18

Group 7

Impulsive	19
Reckless	19
Mischievous	15

Group 7—cont.

Impatient	18
Headstrong	15
Labile	14

Group 8

Amorous	33
Erotic	34
Sensual	33

Group 9

Irresponsible	13
Lax	16
Careless with goods	15
Wandering	15
Conscienceless	17
Easy-going	11
Placid	13

Group 10

Deceitful	10
Dishonest	11
Disloyal	10
Acquisitive	11
Ruthless	10
Hard	11
Cruel	11
Rebellious	10
Selfish	9
Tight-fisted	7

Group 11

Casual	20
Fickle	19

Group 11—cont.
Undependable 21
Quitting 20
Planless 20

Group 12
Conventional 25
Self-distrusting 28
Self-dissatisfied 25
Submissive 22

Group 13
Peaceable 15
Gentle-tempered 15
Humble 15
Trustful 16
Tolerant 13
Naive 14
Unambitious 12

Group 14
Fastidious 24
Faddy 26
Pernickety 26
Pedantic 24

Group 15
Imaginative 19
Musical Aptitude 17
Musical Interests 16
Aesthetic Interests 17
Artistic Interests 17
Drawing Ability 14

Group 16
Hard-headed 11
Shrewd 10
Enterprising 11
Tough 11
Independent 11
Ambitious 11
Decisive 9
Planful 9
Individualistic 9
Worldly 8

Group 17
Interests Wide 19
Leading 15
Versatile 17
Sociable 18
Social Interests 16
Polished 15

Group 18
Intelligent 13
Theoretical Interests 12
Original 12
Verbal Aptitude 11

Group 18—cont.
Mathematical Aptitude 11
Modest 10
Witty 10
Technical Interests 10
Thoughtful 11

Group 19
Pious 16
Reverent 15
Religious Interests 16
Mystical 13
Idealistic 14
Humanitarian 13
Good-tempered 13

Group 20
Alert 21
Poised 20
Clear-thinking 21
Logical 19
Self-controlled 19

Group 21
Hostile 16
Pugnacious 18
Vindictive 17
Slanderous 17
Suspicious 17
Irritable 15

Group 22
Obstructive 25
Ungrateful 26
Mulish 24
Tactless 25

Group 23
Cynical 16
Sarcastic 16
Assertive 18
Argumentative 16
Arrogant 17
Conceited 15

Group 24
Banal 27
Unintelligent 27
Shiftless 24
Narrow Interests 22

Group 25
Coarse 35
Rough 34
Slipshod 31

Group 26
Reserved 21
Taciturn 22

Group 26—cont.
Quiet 20
Shy 19
Self-effacing 18

Group 27
Listless 22
Inactive 21
Leisurely 19
Humourless 19
Mirthless 19

Group 28
Cold-hearted 20
Self-sufficient 22
Secretive 19
Unenquiring 20
Awkward 19

Group 29
Affected 32
Eager for Attention 36
Self-pitying 32

Group 30
Brooding 26
Gloomy 26
Pessimistic 25
Worrying 23

Group 31
Confused 19
Forgetful 22
Disordered in Thought 23
Phantasying 17
Absent-minded 19

Group 32
Dissatisfied 36
Cold 32
Cowardly 32

Group 33
Opinionated 27
Partial 28
Jealous 22
Defensive 23

Group 34
Evasive 21
Extrapunitive 21
Plaintive 19
Egotistical 20
Self-deceiving 19

Group 35
Inhibited 34
Habit-bound 34
Inflexible 32

Method of Scoring

One of the principal objects of this study was to devise a method of simplifying the complex data yielded by the study of an individual personality, so that the result should be capable of statistical manipulation without electronic computing apparatus. The object aimed at was the conversion of the rating on the comprehensive list of 246 variables into a score on a smaller list of compound variables. The derivation of this smaller list of 35 trait groups has been described.

It has been shown that, in using the full list of 246 variables, the only feasible method without an electronic computing machine was to rate for presence or absence of the trait, and use tetrachoric correlations. With only 35 variables, however, product-moment correlations could be used. It was therefore desirable to construct a rating scale for these variables, in place of the "Plus or Minus" method used in connection with the comprehensive list.

Two methods of constructing such a scale were considered. The first was to score each group proportionally to the number of constituent traits rated positive. This was rejected as giving too much weight to those traits having relatively low intercorrelations with other members of the group, and too little to those intercorrelating highly. The method adopted was to weight the constituent traits of a group proportionally to the first factor loading of the trait in the group matrix. For this purpose self-correlations were taken as 1·00 and all correlations below the level of 0·55 were worked out. The first factor loading for each trait was expressed as a percentage of the sum of the first factor loadings of all traits in the group, to the nearest round figure. This figure represents the score for that trait on a 100 point scale. The sum of the weighted scores for those traits rated positive in any given group can then easily be expressed in terms of a scale with any chosen number of degrees. Reduction to a 5 point scale is particularly simple, and a 5 point scale would probably be as convenient as any, if progress to a factorial analysis were contemplated.

The main disadvantage of this method of weighting arises from the fact that, in a group of 3 equally weighted traits, no score of 2 is possible on a 5 point scale numbered from 0 to 4. This defect was considered to be far less serious than the many which would have arisen if some more arbitrary method of weighting had been chosen.

Discussion

To deal at all adequately with the theoretical implications of this study would take up too much space. I have dealt with them fairly fully in the thesis of which this paper is an abstract, so I will now deal only with certain practical aspects of the use of this rating scale.

1. By using punched cards, the weighted score on the 35 compound variables can rapidly be obtained from the original rating on the comprehensive list of 246 variables. The rating on the 246 variables is transferred, for each patient, to a Powers-Samas punched card. A series of master cards, one for each of the 35 groups, is required, with the weighted score for each constituent trait written above the appropriate hole. The cards are superimposed on a black background. The holes representing positively rated traits appear black; it is only necessary to add the figures written above those holes.

2. So far this method of rating has been limited to cross-sectional studies. This was necessary in this preliminary phase of development, but the way is now open to use it for longitudinal studies, by rating individual patients on a number of occasions.

3. This method is intended to supplement, not to supplant ordinary clinical methods of case study.

4. It can form a starting point for further studies, such as Q Technique studies of psychiatric types, or factorial analyses.

5. Finally, this rating scale is particularly intended for use as a rapid yet reasonably comprehensive method of recording psychiatric data in a manner capable of further statistical elaboration. Employed in conjunction with case-records, it should help to make available much information which at present tends to run to waste for lack of a concise and rapid method of codifying data.

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THE PRENATAL PATHOLOGY OF THE CENTRAL NERVOUS SYSTEM

By

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In view of the importance of prenatal pathology at the present time, a useful purpose may be served by attempting to review the peculiar weaknesses and strengths of the developing nervous system. As a result of personal inclinations, this presentation of the various problems involved will have a structural bias; the subject would, no doubt, be approached very differently by a physiologist, for instance, or by a biochemist. Nevertheless we should all be describing different aspects of the same series of phenomena, aiming at an understanding of the events which must occur before the central nervous system can function.

(1) Early Events

The ovum normally becomes fixed, by adhering to the surface of the uterine mucosa, on or about the ninth day after fertilization (Hamilton, Boyd and Mossman, 1945). During the next two days, as a result of proliferation of cells at the point of contact, between the ovum and the mucosa, the embryo sinks beneath the surface of the epithelium. These events are the prelude to an important series of changes, at the completion of which the embryo is provided with a supply of nutrients brought to it by way of the maternal blood stream. Chorionic villi are well formed by the 18th day and it is at about this time that embryonic mesoderm first appears. The embryo is thus, towards the end of the third week, provided with a tissue in which it can form its own vascular system. The amnion and yolk sac appear, at about the same time, as a result of splitting and the formation of cavities in the undifferentiated mass of cells which, on the ninth day, lay at one pole of the blastocyst. These two cavities are separated by a flat plate of tissue, pear-shaped when seen from above, and about $0{\cdot}2 \times 0{\cdot}3$ mm. in size, from which the future individual is obtained.

The nature of the hazards to which the developing ovum may be subject during its first three weeks are not known. It may be surmised that the process of embedding is a hazardous one, although it remains to be shown whether accidents or delays occurring at this stage are in fact followed by disturbances in morphogenesis.

(2) The Fourth Week

There then follows a short period, lasting no more than a few days, during which the foundations of the central nervous system are laid, together with those of the musculature and axial skeleton. The formation of the notochord, neural groove and mesodermal somites are all part of a single co-ordinated

process. By analogy with amphibian embryology, this process is thought to depend on the activity of an "organizer", originating in the first instance from the dorsal lip of the blastopore. Somites first appear on either side of the neural groove in the future neck region; it is from these paired masses of mesoderm that the vertebral bodies develop (Sensenig, 1949). Closure of the neural tube follows, by a process of sealing together of the two lips of the neural plate. Beginning in the thoracic region, the process continues upwards and downwards, leaving a small unclosed gap at either end of the tube, the anterior and posterior neuropore. The posterior defect closes at some time towards the end of the fourth week, a little before the disappearance of the anterior.

The production of a number of important malformations appears to be determined at this time. Among these are: anencephaly and amyelia, cranio- and rachischisis, the Klippel-Feil deformity, spina bifida, the Arnold-Chiari malformation, certain instances of syringomyelia and possibly agenesis of the vermis of the cerebellum. In each of these conditions there is evidence of a failure of structures to fuse in the midline. The best account of the morphological aspect of these anomalies is that of Ernst (1909). The problem of spina bifida has been reviewed by Ingraham (1944), whilst its experimental production in chicks is described by Fowler (1953). Erskine (1946) has dealt with the Klippel-Feil deformity, whilst agenesis of the cerebellar vermis has been studied by Sahs (1941), Verhaart (1942) and Brodal (1945). A personal contribution to the problem of hindbrain and cerebellar deformities associated with vertebral defects in man is now in preparation.

The experimental reproduction of malformations has been achieved in many different ways. Among recent work may be included the dietary experiments of Warkany (1945), those of Gillman, Gilbert and Gillman (1948), using trypan blue by injection into the pregnant rat, and of Ingalls and his colleagues (1950), who induced maternal anoxia. The nature of the anomalous developmental process occasioned by treatment with trypan blue has recently been elucidated by Waddington and Carter (1953). Also of interest are experiments described by Hicks and others (1952), who administered ionizing radiation to pregnant mice. By giving the dose during the first 8 days after coitus (gestation 21 days) Hicks failed to produce malformations of any kind. After irradiation on the ninth day, however, a condition of cranioschisis and anencephaly occurred in a proportion of the foetuses. Similarly, following dosage on the tenth day, foetuses with hydrocephalus, associated with defects in the base of the skull, were characteristically obtained. Making use of the findings of Allen and MacDowell (1940) in normal mouse embryos, it would appear that at the close of the "immune" period on the 8th day, the individuals are normally at various stages between that of the primitive groove and of 4 somites. As a result of histological studies, Wilson, Brent and Jordan (1953) concluded that the anomalies referred to were produced by the effect of X-rays on the mesoderm during the differentiation of the somites. Similarly with regard to human anencephaly, Lichtenstein (1949) suggests that the defect is primarily skeletal, the exposed central nervous tissue being later macerated by amniotic fluid.

From the results of a statistical survey of the occurrence of certain malformations in the Birmingham area by Record and McKeown (1949), and by McMahon, Record and McKeown (1951) it appears that exogenous factors may play some part, also, in determining the production of human anencephaly and spina bifida. Whereas the incidence of these two malformations fell between 1940 and 1947, that of another group, referred to as "hydrocephalus", remained constant during the same period.

(3) Formation of the Cerebral Vesicles

These structures originate from the prechordal extremity of the neural tube at or shortly after the time of closure of the anterior neuropore, at the end of the fourth week, although they do not reach an appreciable size before the 12 mm. stage (six weeks). Whereas the formation of vertebrae and spinal cord depends on the organizing activity of the dorsal lip of the blastopore, that of the olfactory and optic primordia is apparently determined by the mesoderm on which they rest. In experiments on amphibian larvae, Adelmann (1936) and Detwiler and Copenhaver (1941) have shown that, as well as in numerous other ways, cyclopia may be induced by excising part of the prechordal mesoderm, leaving the neural tube intact. It is suggested that the underlying mesenchyme is principally responsible for the induction of lateral paired eyes. If this substrate is absent, diseased or damaged, the production of a cyclops monster results.

In a typical human cyclops there is generally some deformity of the nose, as well as the presence of a single midline eye. On the other hand, absence of the olfactory parts of the brain is an invariable accompaniment and may be the only intracranial abnormality, although there is usually some degree of failure of the two sides of the forebrain to separate, varying from partial fusion of the frontal lobes to the condition of telencephalon medium. Mettler (1947) has emphasized the importance of the occurrence of arhinencephaly in cyclopia, concluding that the normal elaboration of the telencephalon depends on the successful development of the rhinencephalon.

The lamina terminalis, at first the most anterior part of the wall of the telencephalon, originates from the region of the anterior neuropore, after the latter structure has effected the final closure of the neural tube at the end of the fourth week. In this thin sheet of tissue develop the commissural system of the forebrain, i.e. the anterior commissure, corpus callosum and posterior commissure. Failure of the neuropore to close is thought to result in an absence of the whole or of a greater part of the corpus callosum. This is not infrequently an isolated defect, but may also occur with other cerebral malformations, particularly cyclopia, arhinencephaly and allied deformities. The anatomical aspects of the condition of acallosia have been dealt with by Marburg (1949).

(4) Folding of the Cerebral Wall

Despite the apparent complexity of the finished product, the morphological development of the cerebral wall is the result of a relatively simple process by which a pair of vesicles, expanding in a closed space, achieve an increase in surface area which is disproportionately greater than their increase in volume. Growth of brain and skull are parts of a closely co-ordinated process, although unlike that of the spine and spinal cord, it is apparently not regulated by the primary organizer. The results of some recent experiments by Barron (1950) in which parts of the cortex of late foetal sheep were excised in utero, point to the possibility that forces responsible for the folding of the cortex may reside to some extent in the cortex itself.

Gyri normally first appear on the lateral surfaces of the cerebrum between the 12th and 16th weeks of gestation (Connolly, 1940). It occasionally happens that from henceforth the brain simply increases in size, retaining its early foetal proportions to become more or less agyric (Greenfield and Wolfsohn, 1935). Or the growth of the brain and skull may be so retarded that the brain at birth resembles that of a cat, both in size and in complexity of cortical folding. The occurrence of such microcephalic brains has been known to follow X-irradiation of the mother in early pregnancy, as well as maternal rubella.

Changes in shape during development are occasioned by differential rates of growth, the form of a cast of the lateral ventricles neatly outlining the directions in which the cerebrum has expanded. Probably of importance in determining the final morphology of the hemisphere is the fact that an area of cortex, initially at the base of the lateral surface, remains fixed to the thickened part of the cerebral wall which is later to become the striatal region. Consequently the expanding cerebral vesicle either grows away from the fixed area of cortex, forming the frontal and occipito-parietal expansions, or round it, to form the temporal lobe. It is in this way that the insula comes to lie in the depths of the lateral fissure. It is finally covered at the time of birth by opercula or expansions of the frontal, parietal and temporal lobes, which converge over the surface of the buried cortex. The opercula frequently fail to cover the insula in the brains of mental defectives. In the absence of pathological shrinkage of the brain, which may produce the same result, this failure provides evidence of imperfect development of the brain in such individuals. A comparable finding is the frequent occurrence of minor anomalies in the formation of the central and neighbouring sulci in the brains of mental defectives (Berry, 1938).

Le Gros Clark (1945) has emphasized that an important factor determining the sulcal pattern of the medial walls of the hemispheres must be the anchoring effect of the corpus callosum. Presumably following lines of stress occurring during growth, sulci above the corpus callosum tend to run horizontally parallel to its upper surfaces. Where the corpus callosum is absent as a result of malformation or destruction in utero at an early stage, the horizontal alignment of sulci is replaced by a radial arrangement. On the other hand, if as a result of a pathological process the corpus callosum has ruptured or degenerated late in foetal life, the normal horizontal disposition of sulci is usually maintained. This author's views on the extrinsic mechanism of convolutional formation has been criticized by Connolly (1950); similarly, Barron's experimental findings appear to suggest that intrinsic factors determining the pattern of sulci are not absent.

As Le Gros Clark points out, local alterations in the thickness of the cortex appear to determine the sites of formation of the first sulci. Additional factors may be retardation of growth in the cortex as it differentiates, and the early formation of fibres in the cortex and underlying white matter of certain areas, tending to anchor them to deeper parts of the brain. Some personal observations are perhaps relevant to this problem. The central fissure first appears at about the 20th week; in a 28 weeks' human foetus, it has recently been possible to impregnate with silver a dense plexus of neurofibrils in the pre- and post-central gyri and underlying white matter, although this plexus could not be demonstrated elsewhere in the cortex (Dodgson, 1953a).

(5) Formation of the Cerebral Cortex

During the third month of foetal life, intensive mitotic activity occurs in the periventricular cellular matrix of the cerebral hemisphere (Kahle, 1951). Cells formed at this time subsequently migrate towards the periphery through the wall of the neural tube. A proportion of these migrating cells, although avoiding the outermost millimetre or so, reach the margin of the cerebrum, where they accumulate in a densely packed band, from which the cortex later differentiates. Although the details of these cell-movements have been studied morphologically (His, 1904; Mellus, 1912), their significance is not understood.

The formation of sulci and the histological differentiation of the cerebral cortex are two closely related processes. Nowhere is this better demonstrated

than in the microgyric brain (Bielschowsky, 1924), in which more or less of the outer surfaces of one or both cerebral hemispheres is thrown into innumerable tiny folds rather than into the normal deep sulci. In an area of typical microgyria the cortical layer of cells is thin, i.e. there are fewer nerve cells than are normally present. These are arranged in the form of numerous miniature convolutions, each fold corresponding to a corrugation on the outer surface of the brain, although the internal "sulci" are deeper than the shallow fissures on the surface of the brain.

Heterotopic islands of grey matter lying somewhere between the cerebral cortex and the matrix are not infrequently seen in malformed brains. Similar changes are also encountered in the cerebellum when that structure has developed pathologically. Bielschowsky noted the presence of a thin heterotopic lamina of nerve cells immediately below the microgyric cortex. In other circumstances, often associated with anatomical disorganization of the striatum, the central white matter may contain numerous small islands of grey matter, whose production appears to be the result of a distortion of a normally occurring process by means of which the claustrum and parts of the amygdaloid complex are formed. The significance of this pathological phenomenon is not clear; it is not known, for instance whether the heterotopic tissue is formed by the proliferation of primitive cells which have left the matrix, or whether there is an undue persistence of cells which would normally either degenerate (see Glucksmann, 1951) or pass on towards the cortex.

With regard to the causation of anomalies dating from the time during which the matrix is active, there have been many recorded instances of cerebral malformations following pelvic X-irradiation during the early months of pregnancy (Murphy, Shirlock and Doll, 1942). Similar occurrences are known to have followed maternal rubella (Mutrux, Wildi and Bourquin, 1949), and other acute illnesses. On the other hand, in experimental animals, Hicks and his colleagues produced cortical malformations, which are perhaps comparable to the human ones, by subjecting pregnant rats and mice to ionizing radiation and to the effects of radiomimetic drugs and enzyme inhibitors, during the latter two-thirds of gestation. It is possible that in man, as in the experimental animal, developmental disturbances in the cerebral cortex, such as microgyria, may follow damage done to the cell matrix during its phase of active proliferation. An excellent unsigned review on human microgyria has recently appeared (Annotation, 1954).

Excessive proliferation of the cells of the matrix during foetal life may lead to the production of congenital tumours, among which are those seen in tuberous sclerosis (Globus, 1932). The question of the origin of cerebral tumours from cell rests cannot be discussed here. Brzustowicz and Kernohan (1952) have dealt with this problem in regard to tumours of the cerebellum.

(6) Histological Differentiation of the Cerebral Cortex

Although it has long been recognized that there are considerable neuronal deficiencies in the cerebral cortices of idiots and imbeciles (Hammarburg, 1895), little attention has been paid to the possibility of relating cortical function to neuronal patterns. The monumental studies by Conel (1939, 1941, 1947, 1951) of the histological maturation of the cerebral cortex in infancy provide, however, a series of observations on the normal cortex by comparison with which it will be possible to investigate the processes of histological maturation in the brains of infants known to have been subjected to birth trauma, maternal anoxia, haemolytic disease, etc. Such studies may increase our meagre knowledge of the

factors governing the histological maturation in the brain and of the vulnerability of that process. In this connection, the results obtained by Eayrs (1953), who has studied the maturation of the central nervous system in thyroidectomized rats, are of great interest. It is to be hoped that, against such a background, many of the baffling problems relating to the causation and nature of mental deficiency will become intelligible.

(7) The Development of Subcortical Centres

The majority of studies of pathological development arising late in foetal life have been mainly concerned with the cerebral cortex. Involvement of subcortical areas may, however, be equally important; the significance of correlative changes accompanying malformations of its brain has been discussed by Brodal (1946). In a malformed brain studied recently (Dodgson, 1953b), there were areas of partly microgyric, partly overgrown and undifferentiated cortex, which occupied the insular region on either side, encroaching onto the temporal and parietal lobes. Secondary structural anomalies were found in those areas of the thalamus and in the medial geniculate body, to which centres, cortex of the two latter lobes respectively project in normal circumstances. I have recently encountered an example of Gudden's atrophy of the inferior olivary nuclei in two cases showing developmental defects of the cerebellar vermis. Consideration of cases such as these raises the difficult question of the control of morphogenesis and histological differentiation in nerve centres, which is one that remains unanswered by the experimental embryologists, although it is known that in amphibian larvae (Detwiler, 1937) there is a quantitative relationship between the number of anterior horn cells at any level and of nerve fibres reaching them from higher levels. At an earlier stage than that which we are now considering there may be local overgrowth of the neural tube (Patten, 1952), suggesting that unknown growth-accelerating agents may be responsible for abnormal development. This might apply to tuberosclerosis and to certain of the cortical malformations.

The malformations and "congenital atrophies" of the cerebellum have received some attention, although few attempts have been made to elucidate their developmental significance. With regard to the possibility of timing the onset of these lesions, Hicks' experimental results provide a valuable clue. As gestation draws to a close, the rat cerebellum begins to develop rapidly. The effect of irradiation, administered during the last few days of pregnancy and for several days after birth, was to produce necrosis of the outer cortical zones of neuroblasts in the cerebellum, with resulting deficiencies of granular and molecular layers and gross distortion of the folia when the animals reached adult life. An increase in the complexity of the folial pattern, comparable to that seen in the rat, occurs in the human embryo between the 230 and 250 mm. stages, i.e. between the 7th and 8th lunar months (Hochstetter, 1929). Nevertheless, before it is possible to assign the origin of structural anomalies of the cerebellar cortex to this particular epoch of pre-natal life, it would be necessary to know the range of individual variations at which this part of the brain grows and matures. Norman (1940) has described a case in which there was atrophy of the cerebellar cortex in association with état marbré (glial scarring with excessive myelination) of the basal ganglia. The same author, who agrees with the earlier conclusions of Meyer (1926, 1935), has shown that lesions of the latter type, occurring in the area of drainage of the Galenic venous system, may originate at the time of birth (Norman, 1947, 1949). Although the possibility that labour had been premature was not excluded in Norman's earlier case, the coincidence

of cerebellar atrophy with lesions characteristic of birth injury suggests that the developing human cerebellum may retain its peculiar vulnerability beyond the eighth month of foetal life.

Conclusion

An attempt has been made to review the question of cerebral malformations against the background of normal development. Of all foetal tissues, that of the central nervous system is perhaps the most easily damaged following adverse changes in the internal milieu. It is equally unique in the length of time taken to complete its development. There are certain nodal points, e.g. the induction of the spinal cord and vertebral column, and the stage of maximal cellular proliferation in the central matrix, from both of which, if disturbed, a variety of malformations may originate. Nevertheless it is probably true to say that at no time from the third week of foetal life until birth, or later, is the process of normal development absolutely protected. We therefore have, in the foetal nervous system, a sort of clock, by means of which it is possible to time the onset of pathological changes in the foetus.

The incidence of certain of the spontaneously occurring malformations referred to is believed to be genetically determined. Many of these anomalies can be produced equally well by artificial means. In the latter instance, the malformation presumably arises in a hitherto normally developing central nervous system, reacting to an abnormal stress or set of stresses. The possibility must therefore exist that such is also the case with genetically determined malformations, i.e. that these also indicate that a reaction to stress has occurred in an inherently normally developing brain. An adverse change in the internal environment of the brain, may be the thing that is genetically determined; this may not necessarily originate in the foetal nervous system. The fact that there is a malformation of the brain may therefore be incidental, depending on the peculiar vulnerability of that organ during foetal life.

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AN EXPERIMENTAL STUDY OF A METHOD OF USING PERCEPTUAL ERRORS AS AN AID TO DIAGNOSIS

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Introduction

We have at present no reliable method for indicating the correct sequence of treatment in neurotic cases showing a manifold symptomatology. In such cases much time may be lost through attacking superficial rather than basic conflicts. It would therefore be an undoubted advantage to possess a means of indicating objectively and by experiment which problems are fundamental, and to the resolution of which treatment should be first directed.

The work of Rosenstock (1951), devoted to the experimental validation of the psycho-analytic conception of repression, would seem to provide a method, which, when modified for clinical purposes, would provide a means of accurately assessing the neurotic hierarchy of maladjustment. He attempted the proof of the concept of repression by means of a perceptual experiment.

His contention was that, ". . . new perceptions and memories relating to those already repressed can only be assimilated or perceived with a great outlay of energy . . . this expenditure of energy will be proportional to the degree of similarity between the new material and repressed memories—enough energy that is, to overcome the resistance of the field of these memories".

He proposed to investigate this experimentally by formulating and testing the following hypotheses:

"1. Under a sufficiently low degree of illumination repressible material will not be perceived.

"2. Under a sufficiently high degree of illumination this material will be perceived by most subjects. Some subjects may be so affected that the external forces never become great enough to structure the perception in accordance with the stimulus distribution.

"3. Between these two stages there will be areas of uncertainty during which the material will be distorted to a greater or lesser degree. The distortion will be of such a nature as to reduce affect, i.e. in the direction of the perception and report of material less charged with affect.

"4. The threshold for perceiving this material correctly will be greater than that for the perception of material unrelated to previous repression."

In his experiment eight sentences were constructed, four the experimental and four the control. Each was matched and contained 14 words and 18 syllables. The form of each sentence was the same, the second clause containing the affective meaning. The experimental sentences contained sexual and aggressive impulses directed at one or both parents. The control sentences avoided as far as possible sexual and aggressive meanings and comprised other non-pleasant material.

The procedure was for all the sentences to be projected on a screen at seven graded steps of illumination. All were presented at step 1 (minimum illumination), then all at step 2 and so on. To avoid practice effect the slides were presented in random order at each grade of illumination. Each sentence was exposed for 3 seconds. The subjects were allowed as much time as they wished to write down what they saw of each sentence.

The scoring was worked out according to omission of words; one or more words being perceived but insufficient to be scored correct; entire sentence correct.

His conclusions were: "Most subjects see the experimental material only after the external organizing forces become relatively great. It appears that forces exist within the individual which prevent the appearance in consciousness of certain kinds of material, especially sexual and aggressive material."

Method

Rosenstock's work, although directly concerned to objectify psychoanalytic theory, indicates also a method which might be the basis for further experimental investigations into emotional disturbance. It is the contention of this paper that the perceptual disturbance noted by Rosenstock is not specific to sexual sentences only, but applies to all sentences in which disturbing emotional material is involved.

To test the validity of the method, a patient whose case had already received an extensive and detailed clinical investigation was used. The extent of the agreement between the two methods constitutes a test of validity.

Sentences relating directly to the case-history were formulated whilst matched neutral sentences were included as controls. The subject matter involving the most serious disturbance should be clearly differentiated from other material by its giving rise to a significant increase of errors and distortions. The neutral material however would be perceived earlier, at lower levels of illumination and with fewer errors than the affectively loaded ones.

The patient chosen for the experiment had major difficulties in relation to:

1. The parent/child relationship.
2. Correct vocational placement.
3. Sexual adjustment.

The following sentences were constructed with reference to these difficulties:

1. Neutral: The forecast for the winter months in London is one of extreme cold.
2. Vocational: Many do not like menial types of jobs but rather white-collar ones.
3. Sexual: A very large number of people are guilty of very bad sexual conduct.
4. Vocational: He has several times had a change of heart over his life-work.
5. Parent/child: Many people treat their sons more like a child than a grown-up.
6. Neutral: There is a very good film being shown at the Odeon cinema to-day.
7. Sexual: Many people wish that they were not bothered about sex and related matters.
8. Vocational: Working for a living is a necessary evil which we have to tolerate.
9. Sexual: When a man is with a woman he usually thinks of sexual things.
10. Parent/child: Many parents and people find much more fault with children than they should.

Each sentence was matched for the same number of words and approximate level of difficulty. Each was photographed on a 2 in. × 2 in. slide and projected on a screen. The sentences were in black on a white background. The illumination was graded in 7 steps.

The method of scoring is different from Rosenstock's in that every word that is seen correctly is scored as a plus. All incorrect perceptions are scored and included in the final error score. Errors include such as misreading words and including words not in the original sentence.

Procedure

Each of the 10 plates was shown at the same level of illumination before going on to the next. At each higher level the order of presentation was varied to avoid practice effect. There were 70 presentations. Each was exposed for 3 seconds, after which the subject was given as much time as he wished to write down what he saw of each sentence. After each projection the subject folded his paper so as to avoid seeing his previous answers.

The instructions given to the subject were: "This is a test of visual acuity. I am going to present you with a series of sentences which will be projected on to a screen. You will see each one for approximately three seconds. After each exposure I want you to write down what you saw of the sentence. If you cannot read the whole of the sentence and only part of it write down what you saw. I am going to start at the lowest level of illumination and gradually work higher. Are you ready?"

Results

The following are the subject's reproduction at each graded step of illumination. It will be noticed that the order of the sentences has been randomized.

Plate No.		*Content*
Illumination Grade I	1	Neutral (N)
	2	Vocational (V)
	3	Sexual (S)
	4	Vocational
	5	Parent/Child (P/C)
	6	Neutral
	7	Sexual
	8	Vocational
	9	Sexual
	10	Parent/Child

Plate No.		*Content*	
Illumination Grade II	2	V	.....
	4	V	.....
	6	N	.....
	8	V	..... for a ..... evil .....
	10	P/C	.....
	1	N	..... forecast ..... cold.
	3	S	..... very bad .....
	5	P/C	..... frost ..... or crest .....
	7	S	..... they were .....
	9	S	..... is with .....

Plate No.		*Content*	
Illumination Grade III	3	S	A very large number of people are guilty of .....
	8	V	..... living .....
	9	S	..... is with a woman .....
	6	N	..... is very good ..... at the door .....
	2	V	..... special types .....
	4	V	..... several cases had .....

1	N	..... in London ..... extreme cold
7	S	..... they were not .....
10	P/C	..... visit with ..... should.
5	P/C	(Not given.)

Plate No.		*Content*
	4	V	He has several times had a change of heart .....
	9	S	When a man is with a woman ..... sexually .....
	5	P/C	Good parents treat children ..... like sons .....
	2	V	..... like mental types .....
	3	S	A very large number of people .....
Illumination	6	N	There is a very good film on at the Odeon ..... to-day.
Grade IV	8	V	Working for a living is a necessary evil which we .....
	7	S	..... they were not .....
	10	P/C	..... parents and people find ..... fault with the children which they .....
	1	N	The weather forecast for the winter in London is ..... extreme cold.

Plate No.		*Content*
	5	P/C	..... Where parents treat a child .....
	10	P/C	Many parents and people find ..... a child .....
	3	S	A very large number of people are guilty of ..... bad sexual conduct.
	1	N	The weather forecast for the winter ..... in London is ..... extreme cold.
	6	N	There is a very good film being shown at the Odeon ..... to-day.
Illumination	4	V	He had several times had a change of heart over his ..... work.
Grade V	7	S	Many wish ..... they were not bothered about thoughts of sex and money matters.
	2	V	Many do not like mental types of jobs but rather white collar ones.
	9	S	When a man is with a woman he usually thinks of sexual things.
	8	V	Working for a living is a necessary evil which we have to tolerate.

Plate No.		*Content*
	6	N	There is a very good film being shown at the Odeon cinema to-day.
	1	N	The weather forecast for the winter in London is one of extreme cold.
	10	P/C	Many ..... people find ..... fault with children .....
	3	S	A very large number of people are found guilty of ..... bad sexual conduct.
	2	V	Many do not like menial types of job but rather white collar ones.
Grade VI	9	S	When a man is with a woman he usually thinks of sexual things.
Illumination	5	P/C	Many parents treat ..... sons more like a child than a grown up.
	8	V	Working for a living is a necessary evil which we have to tolerate.
	7	S	Many ..... wish ..... they were not bothered about sex and related matters.
	4	V	He has several times had a change of heart over his life-work.

Plate No.		*Content*	
	7	S	Many people wish they were not bothered about sex and related matters.
	10	P/C	Many parents and people find much more fault with children than they should.
	1	N	The forecast for the winter months in London is one of extreme cold.
	5	P/C	Many people treat their sons more like a child than a grown-up.
	4	V	He has several times had a change of heart over his life-work.
Illumination Grade VII	8	V	Working for a living is a necessary evil which we have to tolerate.
	3	S	A very large number of people are guilty of very bad sexual conduct.
	2	V	Many do not like menial types of jobs but rather white collar ones.
	9	S	When a man is with a woman he usually thinks of sexual things.
	6	N	There is a very good film being shown at the Odeon cinema to-day.

The following tables show the correct and incorrect perceptions for each group of sentences at the seven grades of illumination.

TABLE I

Neutral Sentences

Grade of Illumination	Plate No. 1		Plate No. 6		Total	
	Correct	Errors	Correct	Errors	Correct	Errors
1	0	0	0	0	0	0
2	2	0	0	0	2	0
3	4	0	5	1	9	1
4	11	0	10	1	21	1
5	11	0	12	0	23	0
6	13	0	13	0	26	0
7	12	0	13	0	25	0
					106	2

TABLE II

Vocational Sentences

Grade of Illumination	Plate No. 2		Plate No. 4		Plate No. 8		Total	
	Correct	Errors	Correct	Errors	Correct	Errors	Correct	Errors
1	0	0	0	0	0	0	0	0
2	0	0	0	0	3	0	3	0
3	1	1	2	1	1	0	4	2
4	2	1	9	0	10	0	21	1
5	11	1	11	1	13	0	25	2
6	12	0	13	0	13	0	38	0
7	12	0	13	0	13	0	38	0
							129	5

TABLE III

Sexual Sentences

Grade of Illumination	Plate No. 3		Plate No. 7		Plate No. 9		Total	
	Correct	Errors	Correct	Errors	Correct	Errors	Correct	Errors
1	0	0	0	0	0	0	0	0
2	3	0	2	0	2	0	0	0
3	9	0	3	0	4	1	16	1
4	6	0	3	0	7	1	16	1
5	12	0	10	3	13	0	35	3
6	12	1	11	0	13	0	36	1
7	12	0	11	0	13	0	36	0
							139	6

TABLE IV

Parent–Child Sentences

Grade of Illumination	Plate No. 5		Plate No. 10		Total	
	Correct	Errors	Correct	Errors	Correct	Errors
1	0	0	0	0	0	0
2	0	3	0	0	0	3
3	Not given		3	1	3	1
4	3	3	8	2	11	5
5	4	1	5	2	9	3
6	12	0	6	0	18	0
7	12	0	12	0	24	0
					65	12

TABLE V

Mean correct and error perceptions of the four groups of sentences

		Mean Correct Score	Mean Error Score
(*a*)	Neutral	53·0	1
	Sexual	46·3	2
	Vocational	43·0	1·6
	Parent/Child	34·0	6·5
(*b*)	Neutral	53	1
	Affectively loaded sentences ..	41	3·3

TABLE VI

Analysis of Variance of the correct scores to the four groups of sentences

Total Variance of the sub-groups = 1749·978
Total Variance of the groups combined = 1832·435

Variance	D.F.	Sum Square	Mean Square	Variance Ratio
Within groups ..	59	1749·978	29·661	·309 (not significant)
Between groups ..	9	82·457	9·162	—
	68	1832·435		

TABLE VII

Means and S.D.'s of the correct scores per presentation of the neutral, affective and P/C sentences

	Mean	S.D.
Neutral	7·57	4·975
Affective	6·36	5·106
Parent/Child	5	3·742

C.R. between Neutral and Affective Sentences = ·79
C.R. between Neutral and Parent/Child Sentences = 1·49
(Neither is significant)

TABLE VIII

Means and S.D.'s of the error scores per presentation of the neutral, affective and P/C sentences

	Mean	S.D.
Neutral	1	0
Affective	1·625	·854
Parent/Child	2	·818

C.R. between Neutral and Affective Sentences = 1·336
C.R. between Neutral and Parent/Child Sentences = 7·45
(Significant at 1 per cent. level)

DISCUSSION

One important finding emerges from the results. It is that it is necessary to concentrate on error scores rather than correct perceptions. Although the results using correct perceptions are in the direction posited by the hypotheses (see Table V), they are not statistically significant (Table VI). The perception of affectively-loaded sentences seems to result in both a lowered correct-mean score and an increased error score. Both scores seem to be manifestations of the same disturbance though the latter is the only one that can be used experimentally, it alone being statistically significant.

The mean error score of the Parent/Child sentences reaches a level of statistical significance when compared with the neutral mean error score, whilst the mean correct score for the same sentences does not. The explanation seems in part to be that the correct-score means for all groups contain a large number of correct perceptions of non-emotional words. Because these words seem less traumatic they are seen earlier, consequently the means for all the groups are raised, whilst the significance of the differences between them and the neutral sentences is lowered. If only the errors are scored, the non-emotionally charged words are less likely to have any effect.

The incorrect perceptions of the Parent/Child sentences show highly significant results when compared with the neutral ones and argue for this being the area of greatest disturbance. The validity of this conclusion is supported by the results of the detailed clinical exploration supplemented by a later investigation of the patient, involving a home visit, an interview with the father and mother, a visit to his place of employment and an interview with his employer. It pointed to the Parent/Child relationship as the most basic factor.

Perceptual errors seem thus to have been brought under experimental control and shown to be related to a definite emotional disturbance or maladjustment.

Having tentatively shown that a perceptual disturbance occurs and that it seems greater when associated with traumatic material, we need to seek an answer to the question as to whether the formulated hypotheses provide us with a beginning to an explanation of the phenomenon observed.

The excellent reproductions of neutral sentences and the relatively poor perceptions of the affectively coloured remainder point to the following alternative conclusions:

1. The perceptual inferiority is a defensive expedient adopted by the subject against this type of stimulus, i.e. the individual, through distortion and evasion attempts to avoid the disturbing elements in the sentences. If this hypothesis is proved to be correct, we still do not know whether certain individuals adopt other types of defence when faced with the same material.
2. Emotional blockage occurs when disturbing stimuli are presented visually. During the period of blockage no further words are perceived, yet a portion of the 3 seconds allowed for each sentence has passed. There is a consequent reduction of the total number of words perceived. The emotional blockage might possibly result in perceptual distortion, almost in the same way as a frightened and tense pupil, with a teacher standing over him, is incapable of doing his best.

The contribution of several possible simultaneous variables to the incidence and frequency of perceptual errors needs to be investigated. As yet we do not know the effect of embarrassment. The unusual nature of some of the sentences or the experimental design will presumably have an effect. We need to know the extent to which the instrument is capable of evaluating the effects of guilt-feelings, or how to separate this type of disturbance from that caused by embarrassment, if indeed there is a difference. We need to be able to assess the influence of varying degrees of familiarity with the material and the variable levels of subjective confidence which different individuals demand before they verbalize presented "affective" material. In the same way we need to know the influence of certain attitudes such as inferiority or irritability; does a "bravado" attitude reflecting itself in an attempt to master the material result in adequate perceptions of all groups? And finally, whether the subject's perceptions are changed or whether the changes are only in his verbal responses.

Methodological Implications

Three criteria govern the validity of this investigation, using a single case (4, 5, 6). These are:

1. The phenomenon must be brought under control.
2. Precise predictions of behaviour or experience under new conditions must be made possible from the hypotheses which have been developed.
3. Any hypotheses which are formulated must provide a beginning of an explanation for the phenomena observed.

The criterion of "control" has been met in that the increased error scores have been related to a definite area of maladjustment. In other words in proportion as the material presented is non-emotionally disturbing the error scores decrease. With an increase of traumatic content so also is there an increase of error scores.

Likewise definite predictions were made as to the experimental behaviour of the subject. The validity of these hypotheses was confirmed in the case of perceptual errors. They showed a significant increase in an area, commonly agreed after long and intensive investigation, to be the most disturbing.

The beginnings of an explanation of the phenomenon and the possible operation of simultaneous variables have been discussed. Testable hypotheses can now be formulated to give a better idea of the conditions affecting performance. In this way a start will be made in the development of hypotheses which are more specifically concerned with process.

Thus the requisites demanded by experimental investigations of large numbers, i.e. control, predictive power and concern with process, have been met by this single case. Its findings can be considered as equally valid as the results from large numbers. In addition, however, to prove the validity of a method of this kind it is preferable to "overinvestigate" the criterion of validity, rather than be concerned with large numbers, which it would be very difficult to investigate with the same thoroughness.

Summary

It has been shown that a "disturbance" occurs when the subject is asked to reproduce traumatic material projected on a screen. It is reflected in a significant increase of error scores. The error scores are capable of objective measurement.

Having tentatively demonstrated the validity of a method of this kind the main problem appears to be the explanation of the perceptual disturbance. It has been suggested that it is a defensive expedient adopted by the subject. Several other possible variables are discussed.

With greater experimental refinement it is hoped that sentences presented in this way will provide an objective criterion of the relative seriousness of a patient's disturbances. It is hoped that its results will later be able to guide treatment in those patients manifesting a very varied symptomatology.

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CORRELATIONS BETWEEN CHANGES IN MENTAL STATES AND THYROID ACTIVITY AFTER DIFFERENT FORMS OF TREATMENT

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MANY endocrine disturbances have been described as accompanying disturbances in mentation. Single investigations giving a static picture at a certain stage of the disease contribute comparatively little to the understanding of the pathognomonic significance of the biochemical change, even if they are found to be statistically significant.

Longitudinal investigations of the biochemical changes and their suitable chronologic co-ordination to the changes in the mentation should permit more decisive pathogenetic conclusions. Owing to the inherent difficulties connected with biochemical investigations on mental patients, it is a very hard task to accumulate a sufficient number of longitudinal investigation results to decide the degree of their statistical significance. However, such efforts are unavoidable if progress is to be made in psycho-neuro-endocrinologic problems.

In this communication it is proposed to report changes seen in the thyroid function in patients before and after different routine treatment, and in some experimental treatments (not yet in routine use), and to correlate the therapeutic results with the changes seen in the thyroid function. The report comprises observations made in this hospital during the last four years.

Patients

The patients investigated form a fair average of the routine admissions to this hospital. Since it was more interesting for the purpose of this investigation to follow up patients with a thyroid activity outside the normal range on admission, a higher proportion of this group of patients is represented than of those showing an initially normal thyroid activity. The mental state of the patients is recorded in the relevant tables to be found in the following section. The clinical diagnoses were arrived at only after a prolonged period of observation, but were mainly taken from the discharge notes of the patients. The latter contains the diagnosis in the order of the international classification of diseases, 1948. In order to simplify the tables several numbers concerned were often contained in one group. For instance, 301·0, 301·1, 301·2, under the diagnosis "Endogenous depression", or the numbers 303 and 300·3 as "Paranoid schizophrenia". The change in psychiatric state was classified under two headings only; "improved" and "not improved". The criterion for improvement was, whether the patient was well enough to be discharged. It would have been possible to have classified the clinical change under 3 or 4 headings, but for the purposes of statistical evaluation we have found the above method more suitable.

More detailed results concerning some of the endocrine treatment procedure mentioned in this paper are to be published later.

Methods

In all cases the thyroid activity was assessed with an I^{131} tracer method developed in this hospital especially for use on mental patients, Reiss, Hemphill, Murphy, Halkerston and Badrick (1949), Haigh and Reiss (1950), Reiss, Haigh, Hemphill, Maggs, Reiss and Smith (1952) and Haigh, Reiss and Reiss (1954). Thyroid activity was specified in terms of the following measured quantities.

(1) k, the normalized rate of uptake, by the thyroid, of I^{131} during the hour following intravenous injection of the tracer dose.

(2) E_{48}, the proportion of the I^{131} dose excreted in the urine during the 48 hours following the injection.

(3) U_{24}, the amount of I^{131} present in the thyroid 24 hours after the injection.

E_{48} and U_{24} were expressed as a percentage of the tracer dose. A further index of thyroid activity was defined as $I_t = k/E_{48}$, or $I_t = k/(C - U_{24})$, Haigh, Reiss and Reiss (1954), where C is a constant, numerically equal to 91. It avoids the necessity for urine measurements which are the least reliable, especially with mental patients. The uptake measurements were made with Toroidal counters, Haigh (1951) to reduce the effects of unavoidable movements of the patients with respect to the counter.

It has been found that the increased mental tension of some patients, presumably accompanied by an abnormal mobilization of vaso-constrictor substances, appears to inhibit the rate of uptake of I^{131} during the first hour. An anomalously low thyroid activity is then indicated, Haigh, Reiss and Reiss (1954). This difficulty has been overcome by a system of cross-checking the various parameters, and the complete method permits not only the clinically manifest thyroid disturbance to be detected but also tends to disclose borderline cases not easily diagnosed by present methods.

This tracer method has been standardized by measurements on normal control subjects and several thousand hospital patients. With the latter, there was a normal distribution of the logarithmic values of k and I_t (or I_t) and 70 per cent. of the population fell within fairly sharply defined, and hence assumed normal, limits of k and I_t. None of the normal controls gave values outside these limits, Reiss, Haigh, Hemphill, Maggs, Reiss and Smith (1952). However, for simplicity in the presentation of results which follow the characterization of thyroid activity has been restricted to three categories, namely, normal range, above normal and below normal.

Results

E.C.T.

More than half of all the patients investigated were treated with E.C.T. The number of cases improving mentally was of course very high, as only those likely to benefit from E.C.T. were treated in this manner, the selection being made on the basis of the accumulated experience of many years. The results are compiled in Table I, and it can be seen that independent of whether the thyroid activity was below, inside or above the normal range before treatment, there was a strong tendency for E.C.T. to normalize the thyroid activity and it can also be seen how very much normalization and maintenance of the normal state of the thyroid is connected with improvement of the mental state.

TABLE I

E.C.T.

Mental Conditions Treated	Total No.	State of Thyroid Activity before Treatment: Below normal range — No. Patients	Changes after treatment: Unchanged	Further decreased	Increased still below normal range	Increased to normal range	Increased to above normal range	Inside normal range — No. Patients	Changes after treatment: No changes	Changes inside the normal range	Decreased below the normal range	Increased above the normal range	Above normal range — No. Patients	Changes after treatment: Unchanged	Further increased	Decreased but still above normal	Decreased to normal range	Decreased to below normal range
Diagnosis		No.	Improvements					No.	Improvements				No.					
Endogenous depression	80	16	1 1	1 0	3 3	11 11		36	2 2	31 30	2 0	1 1	28	1 0	2 2	6 6	19 14	
Involutional depression	28	6		1 0		4 4	1 1	16	1 1	15 15	1 1	1 0	6			2 2	3 3	1 1
Reactive depression	65	11			4 3	6 6	1 1	38	4 3	30 30	1 1	3 0	16			2 1	14 14	
Schizophrenias (various groups)	12	3				3 3		4		3 3	1 0		5		1 0		3 3	1 1
Paranoic Schizophrenia	6	1				1 1		3		3 3			2		1 0	1 0		
Senile Psychosis	6	1					1 1	3		3 3			2				2 1	
Puerperal Psychosis	4							4		4 4								
Organic Psychosis	4							3	1 0	1 1		1 1	1					1 1
Obsessional compulsive reaction	5							3	1 0		1 0	1 1	2		1 1		1 1	
Anxiety reaction	11	1					1 1	5	1 1	4 4			5				4 4	1 1
Psychoneurosis mixed	3							2		1 1	1 0		1				1 1	
Depersonalization	2	1				1 1		1				1 0						
Immature personality	2	1					1 0	1				1 1						

Group No.	State of Thyroid activity at end of E.C.T.	Total No.	Mental state after E.C.T.: Improved	Not improved	Groups compared	chi²	p
I	Normal range ..	179	169	10	I–III	55·40	$<<0.001$
II	Changing towards normal range ..	27	23	4	II–III	9·60	<0.01
III	Remaining outside normal range or deteriorating ..	25	10	15	—	—	—

For statistical purposes all results are added together and show very significant correlations between normal thyroid activity after treatment ($chi^2 = 55 \cdot 4$; $P < < 0 \cdot 001$) or thyroid activity changing towards normal range ($chi^2 = 9 \cdot 6$; $P < 0 \cdot 01$) and the mental improvement.

C.I.T.

The results of coma insulin treatment are compiled in Table II. Cases treated with C.I.T., in general fall into very different disease entities from those treated with E.C.T.; even so the correlation between mental improvement and normalization of the thyroid occurs after this treatment in the same manner and degree as after E.C.T. Statistical evaluation shows this correlation to be highly significant.

TABLE II

C.I.T.

Mental Conditions Treated	State of Thyroid Activity before Treatment: Below normal range — After treatment: Patients No.	Improvements: Increased to normal range	Inside normal range — After treatment: Patients No.	Improvements: Unchanged	Changed within normal range	Increased to above normal	Above normal range — After treatment: Patients No.	Improvements: Further increased	Decreased but still above normal	Decreased to normal range
Diagnosis	Total No. / No.		Total No. / No.				Total No. / No.			
Schizophrenia (mixed forms)	7 / 1	1 1	3	1 1	2 2		3	2 0		1 1
Simple schizophrenia	2		1			1 0	1	1 0		
Hebephrenic schizophrenic	5 / 1	1 1	1	1 1			3	1 0	1 1	1 1
Catatonic schizophrenic	3 / 1	1 1	1		1 1		1		1 1	
Paranoid schizophrenic	7		7	1 0	4 4	2 0				
Schizophrenic, acute reaction	3 / 2	2 2					1			1 1
Schizo-affective disorder	1 / 1	1 1								

Group No.	Total No.	State of Thyroid activity at end of treatment	Mental state after treatment: Improved	Not improved	Groups compared	chi^2	p
I	19	Within normal range	18	1	I–II	18·90	$< 0 \cdot 001$
	2	Changing towards normal range ..	2	0			
II	7	Remaining outside the normal range or deteriorating ..	0	7			

Modified Insulin

The indications for modified insulin treatment are not yet so well circumscribed as those for the two previously mentioned treatment procedures. The correlation between mental improvement and normalization of the thyroid is equally obvious at first glance, even when, owing to the small number of patients, no proper statistical evaluation was possible (Table III).

TABLE III

Modified Insulin Treatment

Mental Conditions Treated	State of Thyroid Activity before Treatment: Below normal range — After treatment: Patients No.	Improvements: Unchanged	Improvements: Increased to normal range	Inside normal range — After treatment: Patients No.	Improvements: Decreased below normal range	Improvements: Changed within normal range	Above normal range — After treatment: Patients No.	Improvements: Further increased	Improvements: Decreased but still above normal range	Improvements: Decreased to normal range
Diagnosis	Total No.	No.		No.			No.			
Involutional depression	2			1		1 1	1		1 1	
Reactive depression	3			1		1 1	2			2 2
Anxiety state	10	3	1 1	3	1 0	2 2	4	1 0	2 2	1 1
Obsessive compulsive reaction	1						1			1 1

Total No.	State of Thyroid Activity at end of Treatment	Mental State after Treatment: Improved	Mental State after Treatment: Not improved
10	Normal range	10	0
3	Changing towards normal range ..	3	0
3	Remaining outside normal range or deteriorating	1	2

General hospital care and attention, including spontaneous remissions

The thyroid activity of 68 patients was investigated repeatedly during their stay in hospital. These patients received no special treatment during the time of investigation. A number of the patients were not treated as they showed signs of improvement soon after admission, and it was decided to wait in case they showed further signs of spontaneous improvement. They were well cared for, some employed in occupational therapy, others joined the group therapy courses. In twenty-six of the patients ketosteroid excretion was determined several times weekly. In cases where the ketosteroid excretion rate was found outside the normal range, initially, but showed a tendency for normalization during the first ten days, it was decided to withhold any special treatment for a further 10 days, even if there were no immediate signs of mental improvement.

TABLE IV

General Hospital Care and Attention

Mental Conditions		Initial State of Thyroid Activity																		
		Below normal range						Inside normal range					Above normal range							
		Changes after 4–8 weeks						After 4–8 weeks					After 4–8 weeks							
		No.—Patients						No.—Patients					No.—Patients							
		Improvements						Improvements					Improvements							
Diagnosis	Total No.	Unchanged	Decreased further	Increased but still below normal	Increased to normal	Increased to above normal		Unchanged	Changes inside the normal range	Decreased below the normal range	Increased above the normal range		Unchanged	Further increased	Decreased but still above normal	Decreased to normal range	Decreased to below normal range			
	No.							No.					No.							
Endogenous depression	7							3		3 3			4	1 0			3 3			
Involutional depression	2							2	1 0	1 1										
Reactive depression	11	5	2 0		1 0	2 2		5		4 3	1 0		1	1 1						
Schizophrenia (various groups)	9							6	1 0	4 4	1 0		3	2 0		1 0				
Schizophrenia, paranoid	4	2	1 0				1 1						2	1 0	1 0					
Puerperal psychosis	4	1	1 0					1		1 1			2				2 2			
Obsessional compulsive reaction	1							1	1 0											
Unspecified psychosis	3	1		1 0				1		1 1			1				1 1			
Anxiety reaction	19	2	1 0		1 1			12	2 0	9 9		1 0	5	1 1	1 1	1 1	2 2			
Hysterical reaction	2	1					1 1						1				1 1			
Psychoneurosis, mixed	1	1				1 1														
Disturbance of memory	1	1				1 1														
Immature personality	4							1		1 1			3				1 1	2 1		

Group No.	State of Thyroid activity after 4–8 weeks	Total No.	Improved	Not improved	Groups compared	chi^2	p
I	Within normal range ..	43	37	6	I–II	24·81	<0·001
	Changing towards normal range ..	8	5	3	—	—	—
II	Remaining outside normal range or deteriorating ..	17	2	15	—	—	—

It was afterwards seen that these cases showed spontaneous remission, and the thyroid when re-investigated was also in the normal range. The observations are listed in Table IV, the thyroid-normalization: to mental improvement correlation being as highly significant as after E.C.T. or C.I.T.

Leucotomy

Pre-frontal leucotomy was carried out on 16 of the investigated patients, on 5 patients by McKissock's rostral method. Results of investigations are to be found in Table V. There were too few patients investigated for complete statistical evaluation, but the correlation found is equally suggestive as in the previous examples.

TABLE V

Leucotomy

Mental Conditions Treated	State of Thyroid Activity before Treatment											
	Below normal range				Inside normal range				Above normal range			
	After treatment				After treatment				After treatment			
	Patients				Patients				Patients			
	No.	Improvements			No.	Improvements			No.	Improvements		
Diagnosis	Total No.	Unchanged	Increased to normal range		Unchanged	Increased to above normal range	Changed within normal range	Decreased below normal	Unchanged	Decreased to normal range		
	No.				No.				No.			
Obsessive compulsive reaction	2	1		1 1	1		1 1					
Anxiety reaction	4	1		1 1	2	1 0	1 1		1		1 1	
Hysterical reaction	1								1		1 1	
Schizophrenia, mixed forms	8	1		1 0	3	1 0	2 2		4	1 0	3 2	
Paranoid schizophrenia	6	1	1 0		4	1 0	2 1	1 0	1		1 1	

Total No.	State of Thyroid Activity after Leucotomy	Mental State after Leucotomy: Improved	Mental State after Leucotomy: Not improved
16	Within normal range	12	4
5	Remaining outside normal range or deteriorating	0	5

Treatment with Thyrotrophic Hormone

It is instructive to compare the results as seen after E.C.T. in patients with hypothyroidism, with the results of treatment with thyrotrophic hormone. This substance was originally used for diagnostic purposes in order to decide whether the hypothyroidism was a primary thyroid underfunction or a secondary one due to pituitary anterior lobe underfunction (see Reiss *et al.*, 1949). The daily dose injected consisted of 200-600 guinea-pig units (Junkman and Scholler or Heyl and Laqueur) which equal 20-60 USP units. Treatment lasted 2-4 weeks.

Examples of primary hypothyrotic patients are apparently the three patients, the thyroid activity of whom remained outside the normal range, as shown in Table VIII. Such patients were usually treated afterwards with a suitable thyroid preparation and will be reported about in another paper.

Patient material treated and the results are compiled in Table VI. The statistical analysis shows a significant correlation between improvement of thyroid activity and mental state which is in the same grade of significance ($\chi^2=11\cdot01$; $P=0\cdot001$) as seen in the hypothyrotic patients treated with E.C.T.

TABLE VI

Treatment with Thyrotrophic Hormone. (All Patients Hypothyrotic before Treatment.)

Mental Conditions Treated		Changes after Treatment: No. of Patients / Improvements				
Diagnosis	No.	Unchanged	Further decreased	Increased but still below normal range	Increased to normal range	Increased to above normal range
Endogenous depression	4		1 0		3 3	
Involutional depression	1	1 0				
Reactive depression	7			1 0	4 4	2 1
Schizophrenia	2				2 2	
Senile Psychosis	1				1 1	
Anxiety reaction	4				4 4	
Obsessive compulsive reaction	1				1 1	
Hysterical reaction	1					1 0
Unspecified Psychosis	2		1 0		1 0	

Group No.	Total No.	State of Thyroid Activity at end of Treatment	Mental State after Thyrotrophic Hormone: Improved	Not improved	Groups compared	chi²	p
I	16	Normal range	15	1	I–II	11·01	0·001
II	4	Changing towards normal change ..	1	3	—	—	—
	3	Remaining outside normal range or deteriorating ..	0	3	—	—	—

Sex steroid hormone therapy

Treatment with sex hormones was carried out from the following viewpoints:

(*a*) In hypothyrotic patients who also showed signs of other glandular underfunctions, for instance, low 17-ketosteroid or cortin excretion; or failure of the pituitary anterior lobe to produce A.C.T.H. after adequate stimulation.

It was intended in these cases to stimulate the pituitary anterior lobe function by implanting Testosterone crystals (400-600 mgs.) guaranteeing the steady absorption of small amounts of Testosterone which should be sufficient for the purpose.

(*b*) In patients with normal thyroid activity, who showed a decreased 17-ketosteroid or cortin excretion and a negative A.C.T.H. response by the

TABLE VII

Treatment with Steroid Sex Hormones

Mental Conditions Treated	State of Thyroid Activity before Treatment												
	Below normal range				Inside normal range					Above normal range			
	After treatment				Changes after treatment					Changes after treatment			
		Patients				Patients					Patients		
		No.	Improvements			No.	Improvements				No.	Improvements	
Diagnosis	Total No.	No.	Unchanged	Increased to normal range		Unchanged	Changes inside the normal range	Decreased below the normal range	Increased above the normal range		Further increased	Decreased but still above normal	Decreased to normal range	Decreased to below normal range
Endogenous depression	12	3	1 0	2 2	5		4 3		1 0	4	1 0		2 2	1 1
Involutional depression	3				1			1 0		2		1 1	1 1	
Reactive depression	11				6	2 1	3 2	1 1		5			5 5	
Schizophrenias (various groups)	9	1	1 0		3		1 1	1 0	1 0	5	1 0	1 0	3 2	
Paranoic Schizophrenia	5				2		2 2			3			3 3	
Anxiety Reaction	6				3		2 2	1 0		3	1 1			2 2
Depersonalization	1				1		1 0							
Puerperal Psychosis	1				1		1 1							
Organic Psychosis	1									1		1 0		
Immature Personality	1				1		1 1							

Group No.	State of Thyroid activity at end of treatment	Total No.	Mental state after sex hormones: Improved	Mental state after sex hormones: Not improved	Groups compared	chi²	p
I	Within normal range ..	33	28	5	I–II	13·28	<0·001
	Changing towards normal range ..	6	4	2	—	—	—
II	Remaining outside normal range or deteriorating ..	11	2	9	—	—	—

adrenal cortex, the general treatment was Testosterone Propionate 25 mgs. injected daily. In female patients, however, who also showed a prolan I+ reaction in the morning urine, it was found advantageous to combine the injection of Testosterone with 1 mg. Oestradiol daily.

(*c*) In hyperthyrotic patients, in order to find out initially if the overfunction of the thyroid was due to an overproduction of thyrotrophic hormone, high doses of Oestradiol (50,000 to 100,000 units daily) were injected, and if the thyroid activity seemed reduced after a fortnight, secondary hyperthyroidism was assumed and the treatment continued till the thyroid activity was within or below normal range. In cases where complete normalization of the thyroid activity was not achieved the treatment was combined with NaI (100 mgs. daily). In cases showing low ketosteroid excretion at the same time, treatment was combined with 25 mgs. Testosterone Propionate daily.

The disease entities treated, as can be seen from Table VII, were more varied than in either C.I.T. or E.C.T. but the established correlation between thyroid and treatment result was not less significant.

A.C.T.H. Treatment

A.C.T.H. was not given to any cases showing a decreased thyroid activity.

In cases with normal thyroid activity A.C.T.H. was given only when the ketosteroid excretion was very low, the adrenal cortex responsitivity in mobilizing ketosteroid normal, but the ability of the pituitary anterior lobe to mobilize increased amounts of A.C.T.H. after stimulation reduced. Very small doses of A.C.T.H. 2-10 mgs. daily were sufficient to raise the daily ketosteroid excretion of such patients.

In hyperthyrotic patients who showed low ketosteroid excretion rate a positive adrenal cortex response and a negative response of the pituitary anterior

TABLE VIII

A.C.T.H. Treatment

Mental Conditions Treated	State of Thyroid Activity before Treatment: Normal range — After treatment: Patients No.	Improvements: Changed within the normal range	State of Thyroid Activity before Treatment: Above normal range — After treatment: Patients No.	Improvements: Unchanged	Decreased but still above normal	Decreased to normal range
Diagnosis	Total No. / No.	No.	No.			
Involutional depression	2 / 1	1 / 1				1 / 1
Reactive depression	4 / 1	1 / 1	3	1 / 1	1 / 0	1 / 1
Endogenous depression	3		3			3 / 3
Anxiety reaction	1		1			1 / 1

lobe to produce A.C.T.H. endogenously after stimulation, a larger dose of A.C.T.H. (25 mgs. 3-4 times daily) was injected in order to suppress thyrotrophic activity and increase adrenal cortex activity.

Too few patients were investigated in this series to permit any definite evaluation of A.C.T.H. treatment. However, the few investigation results given in Table VIII, suggest the existence of similar thyroid-mental correlations as in the other treatments.

Discussion

1. *The general correlation of changes in mentation and in thyroid activity*

As shown in the preceding section a very significant correlation exists between changes in mentation and the thyroid function. This correlation has been shown to be independent from the psychiatric disease entity or the method of treatment.

Table IX

Survey of all Patients

Group No.	Total No.	State of Thyroid Activity at the end of Treatment	Mental State at end of Treatment: Improved	Mental State at end of Treatment: Not improved	Groups compared	chi²	p
I	324	Within normal range ..	297	27	I–III	162·0	$<<0·001$
II	54	Changing towards normal range ..	40	14	II–III	29·70	$<0·001$
III	72	Remaining outside normal range or deteriorating ..	17	55	—	—	—

The results gained from all the investigations are compiled in Table IX and statistically analysed. It would appear from this analysis that the correlationship mentioned is highly significant indeed ($chi^2=162·0$; $P<<0·001$).

This relationship is also apparent when the patients are grouped according to the initial thyroid function level. In Table X, the results obtained from primary hypothyrotic cases are listed. In 96 per cent. of the patients showing decreased thyroid activity before treatment, the mentation was improved after treatment if the thyroid activity increased to normal range. On comparing this group with the 88 per cent. not improved patients whose thyroid activity remained unchanged or deteriorated, the correlation proved highly significant ($chi^2=48·16$; $P<0·001$). Also, in cases where the thyroid activity was improving after treatment or was already improved, and over-shot (temporarily) the normal range, a significant correlation ($chi^2=9·70$; $P<0·01$) between improvement of thyroid activity and mental improvement can be seen.

Table X

Patients with Initially Decreased Thyroid Function

Group No.	Total No.	Thyroid Activity after Treatment	Mental State after Treatment: Improved	Mental State after Treatment: Not improved	Groups compared	chi²	p
I	11	Unchanged	2	9			
	5	Decreased further ..	0	5			
II	10	Increased, but still below normal range	7	3	II–I	9·70	$<0·01$
	10	Increased to above normal range ..	7	3			
III	59	Increased to normal range	57	2	III-I	48·16	$<0·001$

Table XI shows the changes seen in patients who had an increased thyroid activity before treatment. Here again thyroid changes and mental changes are correlated. A significantly higher proportion of cases improves when the thyroid is decreased to normal range than when the thyroid activity remains unchanged or further increases ($\chi^2=34\cdot66$; $P<0\cdot001$). If the thyroid activity is changed into the normal direction, but has not yet reached the normal range, the relationship still holds but is less significant.

TABLE XI

Patients with Initially Increased Thyroid Activity

Group No.	Total No.	Thyroid Activity after Treatment	Mental State after Treatment: Improved	Mental State after Treatment: Not improved	Groups compared	chi²	p
I	9	Unchanged	3	6			
	15	Further increased ..	5	10			
II	25	Decreased but still above normal range	18	7	II–I	9·09	<0·01
	9	Decreased to below normal range ..	8	1			
III	90	Decreased to normal range	82	8	III–I	34·66	<<0·001

In Table XII results are compiled from patients who had a normal thyroid activity before treatment. It is interesting to note that a deterioration of the thyroid activity of these patients during, or caused by, the treatment does not seem irrelevant for the treatment result. While only 4 per cent. of the patients,

TABLE XII

Patients with Initially Normal Thyroid Function

Group No.	Total No.	Thyroid Activity after Treatment	Mental State: Improved	Mental State: Not improved	Groups compared	chi²	p
I	154	Changed within the normal range ..	148	6	—	—	—
II	21	Unchanged	10	11	II–I	44·16	<<0·001
III	15	Increased to above normal range ..	3	12	III–I	99·83	<<0·001
	17	Decreased to below normal range ..	4	13			

the thyroid activity of whom changed inside the normal range, did not improve, 78 per cent. of the patients, the thyroid activity of whom went outside the normal range during the treatment, remained unimproved. This correlation between the changes in the thyroid activity and the mental state is statistically significant ($chi^2=99\cdot83$; $P<<0\cdot001$). One particularly interesting fact only revealed itself when these tables were compiled: there exists a significant difference in the probability for mental recovery between the patients in whom the thyroid activity showed changes inside the normal range and the patients whose thyroid activity remained completely unchanged. The latter group of patients shows significantly fewer mental improvements than the former. It will be explained further, below, that the changes in the thyroid activity during treatment are only an *indicator* of changes in the hormone equilibrium, which are apparently

correlated to changes in mentation. The fact that changes in the thyroid activity are taking place, even if these changes remain inside the normal range, apparently indicates that changes in total hormone equilibrium are taking place. If, however, no change whatsoever occurs in the thyroid activity, that might indicate that the treatment in question does not influence the hormone equilibrium at all in these particular cases.

2. *Comparison of the effect of different psychiatric routine treatments*

Three years ago, when reviewing the influence of E.C.T. on the thyroid activity (Reiss, Hemphill, Maggs, Haigh and Reiss, 1951) it was surprising to find that the *same treatment* could increase the thyroid activity in patients showing an initially decreased thyroid function, and also reduce a previously increased activity towards the normal range. The explanation was put forward that E.C.T. does not influence the thyroid directly, but interferes with the function of the pituitary anterior lobe and its production or release of the various hormones, thyrotrophic, corticotrophic, gonadotrophic hormones, etc., all these hormones being antagonistic among each other. Thus, in some cases of thyroid underfunction the endocrinologically relevant sequel of E.C.T. consists in an increased production of thyrotrophic hormone which might act either by direct stimulation of the thyroid or by suppression of thyroid antagonistic hormones; while in cases of increased thyroid activity, secretion of more antagonists, such as corticotrophic or gonadotrophic hormone are decisive for the reduction in the thyroid activity observed. In other words: there is no specific influence on the thyroid function by E.C.T.; E.C.T. influences the total hormone equilibrium; changes in the thyroid activity are only an *indicator* for a multitude of changes in the endocrine system taking place after E.C.T. Investigations of changes in other endocrine functions after E.C.T. or other routine treatments, have corroborated this view (Reiss, 1952; 1953; 1954).

A new interesting feature is introduced by the fact that other routine treatments, such as coma insulin and modified insulin therapy show a similar correlation in their effects on the mental activity with changes in thyroid activity as in E.C.T. Quite different psychiatric disease entities, however, are treated with E.C.T. and the other methods of treatment mentioned. The results concerning the change in thyroid activity do not give any clue towards these differences. It cannot be over-emphasized in this connection that the changes in thyroid activity accompanying changes in the mentation are as already mentioned above only *one* indicator that changes in the endocrine equilibrium are taking place. Apart from thyroid activity, the changes in adrenal cortex function and some changes in the function of the sex glands were investigated, but one can fairly say that a considerable part of the endocrine changes taking place are still unknown. Many more investigations will be needed in order to assess the differences between the total action on the hormone equilibrium between E.C.T. and C.I.T.

3. *General hospital care and attention*

The incidence of mental improvement seen in patients who do not receive any special treatment, is of course smaller than in patients who do. It is all the more interesting that in this group of patients as well, there is a very significant correlation between improvement in mentation and thyroid activity. It is well known that very often hyper-thyroidism starts after a psychic trauma. Conrad (1934) has claimed that as many as 94 per cent. of his hyperthyrotic patients revealed a psycho traumatic case history. The epidemic rise of thyrotoxicosis in

Denmark during the last war may also have some connection with possible psycho-traumatic causes (Averson, 1949). It is also generally known how hyperthyroidism and exophthalmos can develop in a very short time after sudden fright. It may be recalled that in the past patients suffering from the less severe hyperthyrotic symptoms were often sent to nursing homes situated perhaps in a mild climate on low mountain sides, where changed environment and nutrition were mainly responsible for the patients return to health. Some of the psychiatric patients too, soon show mental improvement after hospitalization only. The significance of the changes seen in the thyroid function and the improvement of the patients, is still being analysed. It is interesting that in some members of this group of patients, it was possible to predict the coming spontaneous remission by investigating another component essential for the maintenance of the endocrine equilibrium. This was particularly the case in patients who showed increased thyroid activity and very low ketosteroid excretion, the ketosteroid excretion rate starting to rise spontaneously, soon after admission to the hospital (see also Reiss, 1953).

4. *Leucotomies*

Easily recognized endocrine changes after leucotomy are no rarity, particularly in women who after previous amenorrhoea start to menstruate regularly. Some time ago the author observed that a woman who was regarded as eunuchoidal, and was one of the first pre-frontal leucotomies carried out at the Burden Institute, started to menstruate soon after the operation. Hemphill (1944) described enlargement of the testicles in a hypogonadal man after prefrontal leucotomy. The general body weight increase which is also frequently seen after leucotomy is yet another indication that endocrine changes are taking place, the nature of which are not yet completely analysed.

Leucotomy apparently interferes with the supraoptico-hypothalamic, and -pituitary anterior lobe connections. The operation influences, in this way, the pituitary anterior lobe function.

It is therefore, not surprising to find changes in the thyroid activity after leucotomy, these changes being of course, indicators for much more complex changes taking place within the total hormone equilibrium. The psycho-neuro-endocrine correlation seen in leucotomy is the same as in the other treatments in spite of the very different mechanisms of action.

5. *Endocrine treatments*

The rationale of the different endocrine treatments has already been discussed in this paper, together with the evaluation of the results. They were carried out mainly in order to narrow down the range of the possible decisive elements participating in the disturbed hormone equilibrium of the patients.

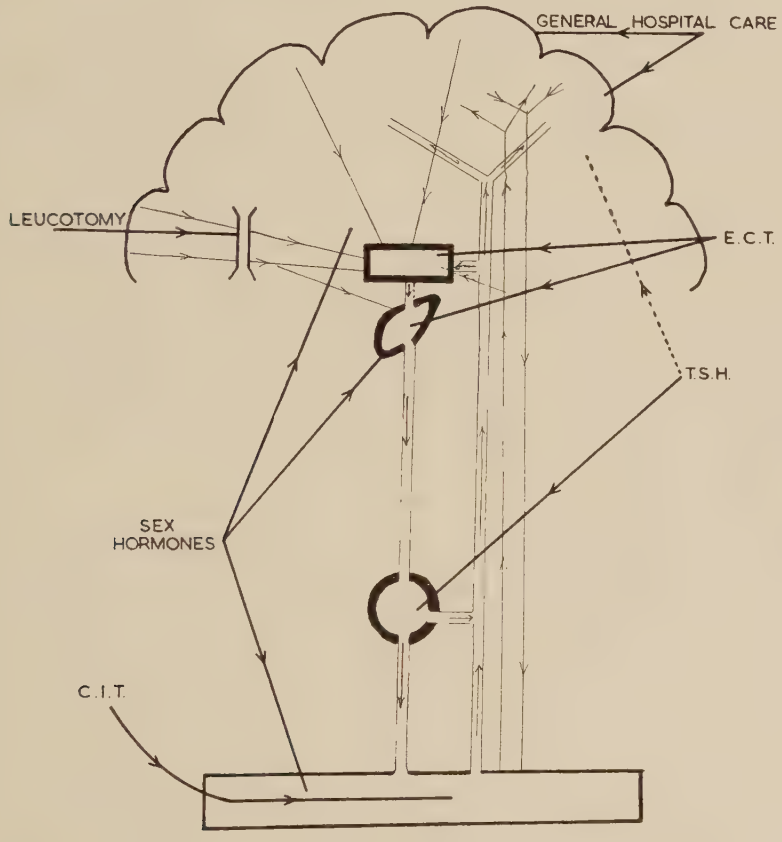
The various shock treatments are still purely empirical and act via a multitude of components, few of them really essential for the mental improvement. In contrast, endocrine treatment appears to be more specific with a narrower range of possible influences on the endocrine equilibrium and mentation. Needless to say, if changes similar to those seen after shock treatments could be brought about by some other, less dramatic, means it might be a great improvement in our therapeutic possibilities. As far as the changes in the thyroid activity as an indicator of the situation in the endocrine equilibrium are concerned, the effect of the various endocrine treatments described in this paper compares favourably, on a statistical basis, with the shock treatments.

It would, of course, be erroneous to arrive at any conclusions regarding

endocrine causes of disturbed mentation, on the basis of these treatment results. Owing to the well known neuro-endocrine interrelationship, most of the endocrine disturbances found during mental disorder, can be either the consequence or the cause of the disease. In the majority of the cases admitted to a mental hospital the disease has already progressed so far that a vicious circle exists, and it is difficult to determine the primary pathological event. From this viewpoint, it will be useful to compare the actions of the different treatments discussed in this paper on the neuro-endocrine axis.

6. *The influence of the various treatments on a psycho-neuro-endocrine circle*

Neuro-endocrine interrelation was extensively described and discussed by the author in this journal (Reiss, 1939; 1944). A scheme illustrating this interrelation, with the pituitary anterior lobe as centre-piece (omitting the posterior lobe) is to be seen in Fig. 1; it is worth considering in order to compare the role



of the different treatments concerned. The scheme shows the physiological interconnection between: Higher Brain Centres—Hypothalamus—Pituitary Anterior Lobe—Peripheral Ductless Glands and Body-periphery, including the relevant centrifugal or centripetal nervous paths, and the humoral connections between the different glands, body-periphery and brain. The physiological interconnection which has been found between these components makes it understandable that a disturbance taking place in any level must upset the whole

neuro-endocrine equilibrium. Increased stimuli of the higher brain centres, as for instance severe emotions or psychic traumata, lead via the hypothalamus to increased production of pituitary anterior lobe hormones (i.e. thyrotrophic hormone) which stimulates the peripheral glands to the secretion of higher amounts of hormones. The latter now act back on the hypothalamus and higher brain centres causing a change in all their activities, among them their regulatory influence on the pituitary anterior lobe. Thus, a pathogenetic cycle of events is set up, becoming progressively worse. Obviously, such vicious circles with a similar pathologic outcome can start in the peripheral ductless gland or the body periphery by most variable stimuli, leading finally to analogous pathologic manifestations as disturbances started after psychic traumata.

It is clear that therapeutic efforts should be directed towards interruption of such pathogenetic vicious circles. This is being achieved by the different treatment procedures discussed above. They interfere, as can be seen in Fig. 1 with the neuro-endocrine circle on quite different planes.

E.C.T. stimulates the brain directly and interferes with the hormone equilibrium by direct stimulation of the pituitary anterior lobe or via the hypothalamus, the latter way being more probable if the experimental deductions of Markee, Sawyer and Hollinshead (1946) and Harris (1952) are correct.

The changes that can occur after change of environment and emotional involvements after hospitalization start on a higher level, in the higher brain centres.

Leucotomy interferes with the supraoptico-hypothalamo-hypophysial nervous connections, influencing the pituitary anterior lobe secretion in this way.

Coma-insulin therapy acts primarily in the periphery, depleting the carbohydrate stores, resulting in a diminution of the blood-sugar concentration. Certain parts of the brain are very sensitive to a reduction in the blood-sugar level, and convulsions occur by a mechanism not yet fully elucidated. The results of this kind of stimulation on the hormone equilibrium are, as far as the regulation of thyrotrophic hormone production is concerned, similar to that achieved by E.C.T.

Treatment with hormones is more circumscribed and direct. Thyrotrophic hormone acts directly on the thyroid, but an additional direct action on the brain or certain brain-parts cannot be excluded if one takes into account the role played by thyrotrophic hormone in the production of exophthalmos.

The sex hormones act on different levels. Small doses stimulate, high doses inhibit, the pituitary anterior lobe secretion. These actions are apparently decisive for the thyroid changes as described above. The action of the sex hormones on the genital tract and their vasodilatory action on the brain capillaries, Reiss and Golla (1940) contribute obviously to appropriate changes in other components of the hormone equilibrium.

Surveying the varying spheres of their interaction with the psycho-neuro-endocrine circle, it is not surprising that the different treatment procedures all act in a similar way in their influence on the thyroid function.

SUMMARY

The thyroid activity of over 400 psychiatric patients was investigated before and after treatment.

A highly significant correlation was found between a normal thyroid activity after treatment and mental improvement, or, thyroid activity outside the normal range and non-improvement.

This correlation held good in all the disease entities investigated and was independent of the treatment applied.

Changes in the thyroid activity measured are regarded mainly as indicating more extensive changes in the total hormone equilibrium of the patient.

The action of electroconvulsive shock therapy, coma insulin therapy, treatment with thyrotrophic hormone, treatment with steroid sex hormones, of leucotomy and of general hospital care and attention, on the psycho-neuro-endocrine circle are discussed. The various forms of treatment act in different levels of the neuro-endocrine regulatory system, but their final result appears to be the same as far as the hormone equilibrium is concerned.

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THE FRACTIONATION OF URINARY NEUTRAL 17-KETOSTEROIDS FROM CHRONIC MALE SCHIZOPHRENICS

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Investigations carried out in the past into the steroid hormone excretion rate of mental patients have been limited to the quantitative determination of the total compounds. Assay of neutral 17-ketosteroids in particular, has revealed no significant difference in the excretion rates of schizophrenics from that of normal controls (Leth Pedersen, 1947; Lingjaerde and Lierasylet, 1949 *et al*). Pincus (1943) has studied the diurnal excretion pattern of 17-ketosteroids in normal persons; a different pattern was shown to occur in some schizophrenics (Reiss, Hemphill, Gordon and Cook, 1949). Some schizophrenic patients also show considerably greater fluctuations in the 24-hour excretion rate than normal persons (Reiss *et al.*, 1949), these fluctuations disappearing after successful treatment of the patients (Reiss, 1952). An increased percentage of excreted 3 β–hydroxy–17–ketosteroids has recently been reported (Mittelman, Romanoff, Pincus and Hoagland, 1952) in schizophrenics compared with normal people, the total ketosteroid excretion rate being found similar in both groups. Increased β–ketosteroid excretion rate was also seen by Reiss, Hemphill, Gordon and Cook (1949), during depressive phases in a state of manic depressive psychosis.

However, no satisfactory or final insight into the function of the adrenal cortex or gonads during mental disturbance, can be gained as long as the only information is that concerning the total steroid excretion rate. Results of systematic investigations dealing with the qualitative aspects of this subject are practically unknown in the literature. Differences in the patterns of excretion of the various individual ketosteroids may occur although the sum total of these compounds can appear within the normal range. For this reason, urinary neutral 17–ketosteroid extracts from mental patients have been fractionated in this laboratory during the past years by different chromatographic methods. Most of the methods used, however, have proved unsatisfactory for routine investigations on a large scale. A partition chromatographic method developed during the last two years (Jones and Stitch, 1953) has proved to be satisfactory. In this paper the authors report some significant differences found, so far, between the ketosteroid excretion patterns of schizophrenics and normal persons.

Patients

The series investigated consisted of all types of schizophrenic illnesses, apart from catatonics. All the patients may be regarded as chronic, not in

remission, their hospitalization ranging between one to twenty-six years. The patients are not recorded separately according to hospitalization time, since no difference whatsoever could be found in the excretion rate (to be described later) on the basis of hospitalization time. The patients were only split into two age groups as can be seen in Table II, but even between these groups no significant difference could be shown.

The control persons investigated consisted of members of the laboratory staff. During the period of the urine collection the patients were watched very carefully by the nursing personnel and the determination of creatinine excretion was in any case carried out as well in order to control the completeness of the urine specimens.

Chemical and Investigation Methods Used

The urines were hydrolysed and the 17–ketosteroids extracted according to the method of Callow, Callow and Emmens (1938) and the ketonic fraction separated with Girard's reagent "T" (Girard and Sandulesco, 1936). Aliquots of the ketonic material (2·5 mgs. approximately) were dissolved in the mobile phase—light petroleum (boiling range 60°–80°) containing 3 per cent. chloroform, saturated with nitromethane. The extracts were then fractionated by partition chromatography on columns of silicic acid containing nitromethane as stationary phase (Jones and Stitch, 1953).

The effluent from the columns was collected with the help of a fraction cutter (Grant and Stitch, 1951) in fractions (5 ml. approximately) transferred to 6 in.$\times\frac{5}{8}$ in. Pyrex test tubes and evaporated to dryness. Unglazed stone particles were added to assist boiling and the last traces of solvent were evaporated under reduced pressure from a water pump at 100° C. The ketosteroid content of each tube was estimated by means of the Zimmermann reaction, and peaks were observed corresponding to the position of known substances. It is not possible to say that each peak represents one substance only.

Typical chromatographic patterns are shown in Fig. 1 and the substances known to occur in the chromatographic peaks are shown in Table I.

Table I

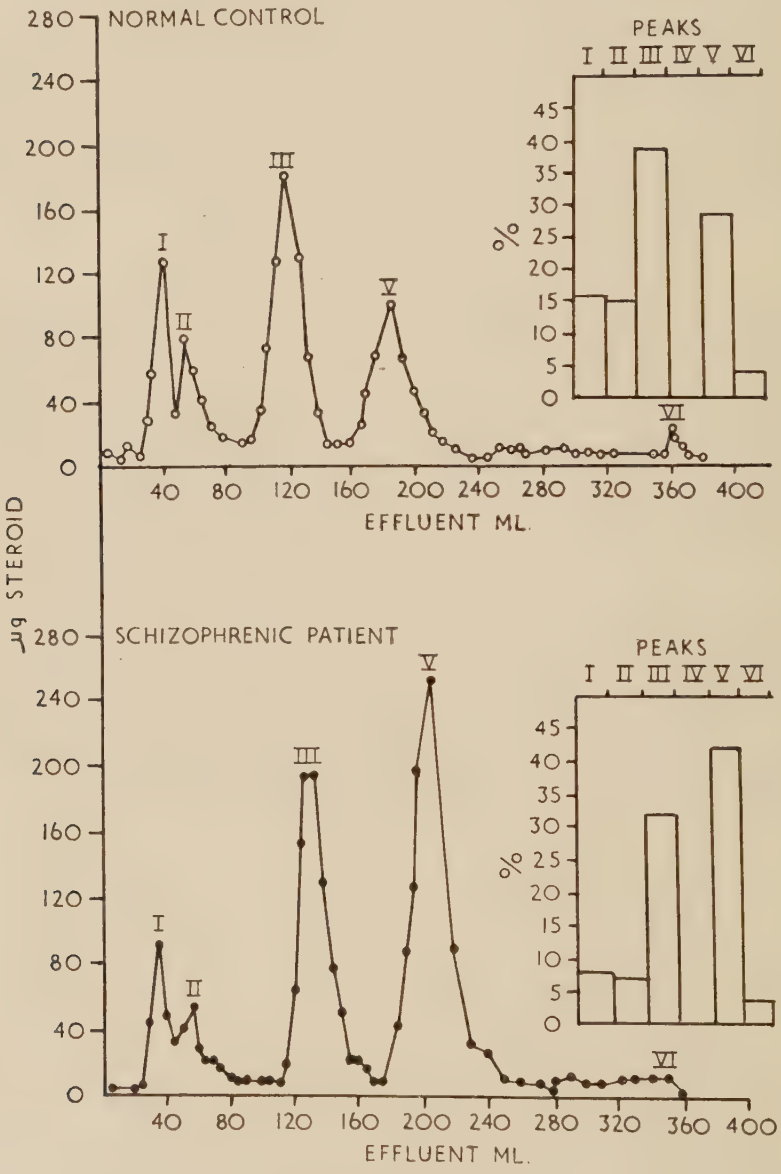
Substance	Peak No.
3–β–chloroandrost–5–en–17–one	1
Unknown	2
Androsterone	3
Androstan–3β–ol–17–one	4
Androst–5–en–3β–ol–17–one Teston–3α–ol–17–one	5
Androst–4–en–3,17,dione Polar 17–ketosteroids	6

The position of the 11–keto and 11–hydroxy–17–ketosteroids on the chromatograms is not known with certainty. Peak 1, 3–β–chloroandrost–5–en–17–one, is an artefact derived from androst–5–en–3β–ol–17–one. We have, therefore, added Peak 1 to Peak 5 in the results in order to give a truer picture of the 17–ketosteroid excretion.

Results

It can be seen from Fig. 1 that the relative amounts of Peaks 3 and 5 are somewhat different in the schizophrenic and the normal person. In normal persons Peak 3 (androsterone) is higher than Peak 5 (Androst–5–en–3β–ol–17–one+Teston–3α–ol–17–one) while in schizophrenic patients the

relation is the other way round. This difference has been found in a number of cases and has been shown to be significant.



A summary of the results gained from relevant data obtained from all the patients and normal control persons is shown in Table II and a statistical evaluation of Table II is shown in Table III. The tables show that significant differences exist between the controls and schizophrenics investigated for the ratios of Peaks 5 : 3 and (1+5) : 3 at $P=0{\cdot}05$ and $P=0{\cdot}01$. The excretion rate of the individual fractions is also shown to be significantly different. It seems that normal controls excreted significantly more androsterone than chronic

TABLE II

Subjects	No.	Age Range	Age Av.	No. of investigations	17-ketosteroid excretion Mg/24 hours Range	17-ketosteroid excretion Mg/24 hours Av.		Chromatographic Fractions: Peaks: In Percentage of Ketosteroid Excreted: 1	2	3	4	5	6	Ratio of Peaks: 5:3	(1+5):3
Normal Controls	9	21–61	27·5	11	5·0–16·7	9·7	Range	9·0–22·0	0·0–13·8	22·0–50·0	0·0–2·0	17·0–32·7	2·0–18·4	0·40–1·36	0·64–2·14
							Av.	14·8	5·7	38·6	0·29	24·9	8·2	0·70	1·12
							S.D.	±4·0	±5·1	±9·0	±0·7	±5·8	±5·4	±0·31	±0·47
Schizophrenics Group I	7	19–35	26	9	4·3–16·8	8·7	Range	17·5–26·0	2·4–8·4	13·3–29·5	—	28·0–43·6	2·7–9·7	1·08–1·72	1·47–2·4
							Av.	15·2	5·7	26·4	—	35·8	6·6	1·37	1·99
							S.D.	±7·6	±2·1	±5·1	—	±6·5	±2·3	±0·23	±0·46
Group II	10	36–59	47	11	2·9–16·0	8·4	Range	3·0–21·4	1·7–11·9	20·8–37·5	0·0–2·4	27·7–46·0	2·7–5·0	0·95–1·85	1·13–2·36
							Av.	11·1	6·0	29·3	0·43	34·3	3·4	1·20	1·61
							S.D.	±5·8	±3·4	±5·7	±0·91	±6·0	±1·5	±0·28	±0·37

TABLE III

Statistical Evaluation of Table II

Comparison of "t" value in relation to normal controls

Group	Value of "t" for chromatographic peaks		Value of "t" for ratio of peaks		Value of "t" required for significance at probability of		
	3	5	5:3	(1+5):3	0·05	0·01	0·001
I	3·39	3·51	4·96	3·72	2·15	2·98	4·14
II	2·66	3·47	3·57	2·51	2·11	2·90	3·97

schizophrenic patients (P=0·01) and less of the substances contained in Peak 5 (Androst–5–en–3β–ol–17–one+Teston–3α–ol–17–one) (P=0·01).

There is practically no difference between the younger and the older age group of the schizophrenics; the results of the latter showing a difference in Peak 3 which is only significant at P=0·05. In schizophrenic patients the range of the 24-hour excretion rate starts below that of the normals, particularly in the older age group, but the averages are not significantly different from the average excretion rate of normal controls.

DISCUSSION

The sum of Peak 1 and Peak 5 should contain the total of the excreted 3–β–hydroxy–17–ketosteroids in addition to etiocholanolone (Teston–3 α–ol–17–one). If the higher values for Peaks 1 and 5 observed in the schizophrenic group represent an increased excretion of 3–β–hydroxy–17–ketosteroids this finding is in good agreement with that reached by Mittelman, Romanoff, Pincus and Hoagland (1952) who used other, comparatively simpler methods for their investigation, and who also apparently did not analyse complete 24-hour urine specimens.

The investigation results described above show that the disturbance in the equilibrium between the different excreted ketosteroid fractions goes even further. The androsterone excretion rate is significantly lower in the schizophrenic patient group as compared with the normal controls. It might be added that this disturbance occurs comparatively early during the disease. The authors have also investigated the urine of some young schizophrenic patients who, according to clinical investigation and careful enquiries, were reliably acute schizophrenics. They showed, even at this early stage, the same ketosteroid chromatogram as described as characteristic for chronic patients. The differences were occasionally even more pronounced, one of them showing no androsterone excretion at all. It has not yet been possible to include these patients in the statistical evaluation and they will be reported on at a later date.

It would be useless at the present stage to dwell on considerations of the causal relationship between the psychiatric symptoms and the biochemical findings. One can only start to do so if a change in the excretion pattern, reached through different ways of treatment, could be accompanied or followed by mental improvement. This should be rather easy to verify since the percentual participation of the different steroid compounds in the total ketosteroid excreted remains very constant in both controls and patients over many months; in the latter especially, even if the excretion rate of the total 17-ketosteroids fluctuates a great deal. Unfortunately such longitudinal investigations are, owing to the time taken by the rather complex analysis of every single urine specimen, very time-consuming and it might take years before proper statistical evaluations of a multitude of such longitudinal investigations will be possible.

Hemphill and Reiss (1948) and Reiss (1953) reported some time ago about changes in the excretion rate of the different ketosteroid components in catatonics on the basis of investigations carried out using an absorption chromatographic method. They were able to show, an apparently causal relation between the excretion of the β-ketosteroid dehydroandrosterone, and mental improvement.

The relation between adrenal cortex function and schizophrenia is at present being discussed very intensively. There is, of course, no doubt that in some cases, as described by Broster, Allen, Vines, Patterson, Greenwood, Marrian, Butler (1938), and Allen, Broster, Vines, Patterson, Greenwood, Marrian and Butler (1939), where the removal of an adrenal cortex tumour lead to an improvement of the mental state, the rôle played by the increased adrenal cortex activity was to a certain extent in a causal relationship with the development of the mental disturbance. However, the total endocrine equilibrium of the described patients ought to be given closer consideration. The description of the cases in question shows that adrenal cortex hyperfunction must have existed for a long time, but does not permit any conclusions about the secondary endocrine changes, particularly of thyroid and pituitary, which might equally well have been the cause for the psychopathologic phenomena. In any case such results cannot be used as a basis for generalized claims about the causal importance of adrenal cortex over-function in the development of any mental disturbance.

Specific claims made by Altschule (1953) in this direction appear to be quite unfounded. The main basis for his claims of the causal importance of adrenal cortex hyperfunction in schizophrenia is the eosinopenia seen during the disease and of the rise of the eosinophils during remission. Such claims cannot be maintained, since it is now well known that adrenaline decreases the blood eosinophil count even after adrenalectomy, acting directly in the periphery. On this basis it would seem that the increased tension of certain psychiatric patients which, as is known, is accompanied by an increased mobilization of adrenaline, is the direct cause of eosinopenia, while disappearance of the tension and anxiety is connected with a rise and normalization of the blood eosinophil count. It has recently even been shown that the levels of the blood eosinophils and lymphocytes can be influenced by other mechanisms than the pituitary-adrenal system, as, for instance, by treatment of adrenalectomized rats with dicarboxylic amino acids (Harris and Lang (1952)). It is necessary to emphasize these facts since, on the basis of assumed general over-function of the adrenal cortex, adrenalectomy of schizophrenic patients has been advocated, a procedure which is at present not justified. It also appears somewhat illogical if one considers that, with the removal of the adrenals, an organ important for some processes of adaptation is being removed. On the other hand, under-function of the adrenals, too, has been claimed as a basis for development of schizophrenia and other mental disturbances, and Bleuler (1951) and Cleghorn (1952) do not see an essential difference between the psychopathologic manifestations accompanying adrenal cortex under-function or over-function.

It seems that the results described in this paper come much nearer to the truth in the matter discussed. Neither over- nor under-function of the adrenal cortex, as such, can be related causally to specific psychopathological changes. One has, moreover, rather to deal with a disturbed equilibrium in the production of the different steroid hormone components of the adrenal cortex amongst themselves and most probably between the steroid hormone production of adrenal cortex and gonads. Considerable effort is still needed in order to elucidate the very complex relationships.

This paper deals with the ketosteroid excretion of schizophrenic patients

only. It should by no means be claimed that the described disbalance between the different components is significant in schizophrenia only. Investigations of the fractionated ketosteroids in other disease groups are still in progress.

Summary

Fractionation of the 17–ketosteroids excreted during 24-hours in normal male and chronic schizophrenic male subjects was carried out.

Significant differences in the chromatographic patterns obtained were observed, chiefly differences in the relative excretion of some fractions which are discussed.

The possible relationship between the biochemical findings and psychopathologic phenomena are considered.

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TUBEROSE SCLEROSIS TREATED BY DEEP IRRADIATION

By

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(Received 28 February, 1954)

Epiloia occupies an intermediate position between the neoplasms on the one hand and other diseases, such as Huntington's chorea and Tay-Sachs disease, which are system disturbances, presumably based on a metabolic disorder. The lesions in the disease-complex of epiloia might at first sight appear mainly neoplastic in form. Thus the brain nodules have the form of gliomata. Polycystic kidneys may be classed as neoplastic (Jeanbrau, 1928; Vines, 1949). In some cases a frank hypernephroma may develop (Kirpicznik, 1910; Berg, 1913; Ferraro and Doolittle, 1937). The rarely encountered heart lesions may take the form of rhabdomyomata, whereas the skin lesions of the face which are pathognomonic of the disease are described as sebaceous adenomata (Figs. 1 and 2), i.e. benign neoplasms of the sebaceous glands of the face in the area to either side of the nose. In fact the facial eruption is seldom simply adenomatous but is complicated by elements of an angiomatous or warty nature. The heart lesion may likewise involve a variety of elements.

Some of the abnormalities which are less commonly found in epiloia are definitely not neoplasms. This particularly applies to the form of the disease which shades off into von Recklinghausen's disease (e.g. the mother of Dickerson's cases 4 and 5) and which is characterized by "café au lait" patches of skin pigmentation or by "peau de chagrin". The latter condition, however, is not unlike some pre-cancerous states of the skin.

A fundamental difference between epiloia and most neoplasms is that the majority of the tumours found in this disease are present at birth although often manifesting themselves later (Stewart, 1935). This does not apply to the skin eruption on the face, which usually appears between the 3rd and 8th years of life. A second difference lies in the fact that in full blown cases of the disease a vast number of tumours are present whereas the majority of neoplasms are initially solitary. In this respect epiloia may be likened to conditions such as Hodgkin's disease or to multiple tumours of known infectious origin such as those of verruca vulgaris or molluscum contagiosum. The similarity to the latter condition lends support to the suggestion made by Professor Penrose that epiloia may be at least in part a reaction to a virus infection, rather than being, as commonly suggested, wholly explicable as determined by a Mendelian dominant character, partially expressed.

The former hypothesis could also be used to explain the fact that epiloia, unlike most neoplastic conditions, has a familial tendency in some cases, re-appearing, though in very diverse forms, in two or even three generations (Dickerson, 1951; Marting, 1941). Shelmire (1918) has recorded adenoma sebaceum in 5 members of one family. On the analogy with certain plant diseases (Cayley, 1928) it can be assumed that a placenta-passing virus affects

FIG. 1.—Patient D.J. showing typical distribution of adenoma sebaceum in "butterfly"-shaped area.
Photographed by Dr. L. Crome.

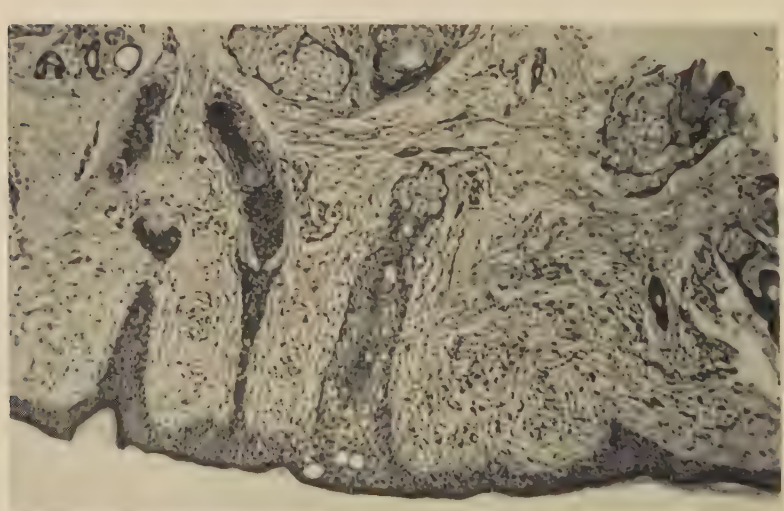

FIG. 2.—Section of rash of adenoma sebaceum from patient D.J. showing that the hypertrophy of the skin is by no means confined to sebaceous elements.
Photographed by Dr. L. Crome.

the new individual at an early stage in development, thus accounting for conditions which are thought to be hereditary. The suggestion advanced by Quill and Marting (op. cit.) that given forms of epiloia, e.g. with sub-ungual tumours, are inherited, does not conflict with this suggestion, since a similar problem occurs in syphilis where the neurotropic variety appears in members of one family (Moore, 1947). It may be possible to test this hypothesis by animal inoculation.

Another difference between the tumours of epiloia and common isolated tumours is that the former have little tendency to grow. This is true in general, but there are exceptions to the rule. The disease indeed may occasionally present with the classical picture of a cerebral neoplasm (e.g. the mother of Dickerson's cases 4 and 5). The established case of epiloia in this static form may occasionally be complicated by symptoms suggestive of a growing cerebral tumour.

These considerations led to the view that it would be logical to attempt the treatment of certain cases of epiloia by means of deep X-ray therapy. One of the difficulties which confronts the treatment of this disease is that the majority of the patients are either hopeless idiots or suffering from such a mild, abortive form of the disease (e.g. the mother of Dickerson's cases 1 and 2, see also Walsh, 1947), that such drastic treatment as deep irradiation is not indicated. None the less in those of its victims whose condition is threatened with deterioration as a result of increase in size of one of the gliomatous masses, such treatment, it was considered, should be tried, especially in view of a report by Friedman (1939) who states that after irradiation of the head of a patient with tuberose sclerosis fits ceased for at least two and a half years, the patient remaining normal mentally and working as a clerk. He used in the first stage of treatment "a total dose of 850 r to each of 4 fields". In the second stage "850 r in divided doses to each lateral field". Kessel (1949) recommends that any surgery in tuberose sclerosis should be followed by X-ray therapy. In the case of Koch and Walsh (1939) irradiation was administered but the patient, after 7 months, was no better. This, however, was a case where the patient had become almost completely blind before treatment.

Case Report

This case was reported briefly previously prior to treatment (Kirman, 1949).

D.J., born 6.iv.40. Male.

The patient is the only member of the family known to be affected by the condition. There is no family history of epilepsy, mental defect or adenoma sebaceum. The father is a road-sweeper, the mother a charwoman. The home is a poor one. The parents are in good health. The patient is the last-born of five. The siblings are as follows (1952):

1. Girl, died at 6 years of diphtheria.
2. Boy, died at 4 years of diphtheria.
3. Boy, aged 15, at work.
4. Boy, aged 14.
5. Patient.

Both parents were aged 42 at the patient's birth. The mother was well during pregnancy. The birth was quick and easy. Birth weight was 9 lbs. He was bottle fed. At 12 months he walked and at 15 months is said to have talked. No abnormality was noted until 18 months when he began to have epileptic fits for which he was taken to hospital. He is said to have been unconscious for two days. The parents attributed the fits to the explosion of a land mine. He is said to have teethed normally, to have become clean in his habits and to have learnt to use a spoon prior to admission to the Fountain Hospital.

He was admitted 27.ix.45. At that time he was already said to be deteriorating both mentally and physically. He could not wash or dress and had frequent attacks of petit mal. He said only a few words. He knew his name but not his sex or age. He could not copy a straight line or match colours. After admission he was found to be faulty in his habits. He could walk well and wandered round the ward although there was a left talipes equino-varus with left hemiparesis. The Wassermann Reaction and parallel test were negative. The cerebro-spinal fluid showed 7 lymphocytes per cubic millimetre, 35 mg./100 cc. protein, negative Wassermann reaction and Lange test.

Soon after admission he had a succession of fits, going into status epilepticus. He continued to have both major and minor attacks. He was able, however, to attend the occupation centre where at first he made some slight progress though his mental level was noted to vary from day to day—possibly owing to sub-clinical fits. In 1946 the rash of adenoma sebaceum was noticed, beginning with a patch of partial baldness with induration of the scalp, followed by a lesion with a typical paranasal distribution.

In 1947 he was still able to walk though unsteadily and on a broad base. He talked to other children and occasionally answered questions from the staff. He could use his paretic hand a little. An electro-encephalogram (E.E.G.) showed an abnormal record with irregular dominant delta activity. Some "sharp waves" were seen in the posterior areas of both hemispheres where the greatest abnormality was found. The delta activity had the greatest amplitude and slowest frequency in the left occipital lobe.

A radiological examination of the skull showed a small calcareous deposit in the left hemisphere.

In August, 1947 a rapid deterioration occurred following a series of fits. He was then found to have a paresis of the right (i.e. his good) hand which had now become almost useless. His gait acquired a high-stepping character. He became very ataxic, appeared dazed and could not understand anything said to him. A month later the right hemiparesis was worse than the old established left weakness. From that time on he never spoke again. He made efforts to feed himself with his left hand but these were unsuccessful.

An eye examination at that time showed a phakoma over the left macula.

At this stage deep irradiation was suggested but the view of the radiotherapist, who was consulted at that time, was that the tumours would probably be completely insensitive and that the treatment would inflict "unnecessary discomfort on the patient". (This was not the view of Dr. R. M. Patterson who saw the patient at a later stage.)

Deterioration continued. He became doubly incontinent and unable to walk without assistance, though he still showed his tongue on request and was delighted to be allowed to scribble with a pencil on request. In 1949 he had a complete right hemiplegia with considerable paresis on the left side.

In March, 1949 he received 2,000 r on alternate days 4 doses on each side to each motor cortex. This therapy was given at Charing Cross Hospital at the suggestion of Dr. Frank Elliott under the direction of Dr. R. M. Patterson. In April, 1949 he showed no particular change. He made a poor attempt at walking. He appeared very lethargic. He was spoon-fed and made no shift to obey simple instructions. On the Merrill-Palmer Scale he scored an I.Q. of 18 and on the Stanford-Binet 20. When tested he was friendly and tractable. He made some slight effort at speech. Subsequent testing showed little significant change.

In May, 1949 the E.E.G. report from the Maudsley Hospital was as follows: "The whole record remains grossly abnormal. The dominant activity is of slow irregular delta waves which show poor organization over the whole cortex, save for a tendency for the waves to be sometimes bilaterally synchronous. Traces only of normal alpha activity are seen. The record suggests a gross generalized cortical disturbance, possibly secondary in the main to some cerebral lesion." The record was found to bear some resemblance to those of cases of sub-acute encephalitis.

Present Condition

He remains a low grade imbecile. He still does not talk. His comprehension is very limited. With his good hand (the left) he will point to his nose, chin and hair on request, but not his ears. When asked to point out another patient mentioned by name, he does not do so. He can feed himself with the left hand. He is clean in his habits if supervised. He cannot walk. Physically he is a cripple with spastic diplegia, more marked on the right. Both feet are held in equinus position. At thirteen he is excessively fat and heavy (Fig. 3) though in good general health. The adenoma sebaceum, as is usual at the age of puberty, has become more obvious with dilatation of the superficial blood vessels. The blood pressure is 110/74. The urine contains a very faint trace of protein and on culture there is a heavy growth of streptococcus viridans and of staphylococcus albus. The blood groups are as follows:

ABO	Rh	MN	S	P	Lewis	Kell	Lutheran
A_1	R_1r	N	−	+	−	−	−

The record of epileptic fits is as shown in the accompanying diagram. He received small doses of phenobarbitone intermittently in 1948 and 1949 but no other medicine.

Comment

In the present case no benefit resulted from the treatment apart from a reduction in the number of fits which may be a coincidence. It may be, however, that if treatment had been given earlier, when it was first suggested, irreversible destruction would not have taken place. Clearly, in any such case treatment should be given as soon as it is decided that it is indicated. Only in this way can an estimate of its value be explored. The development of symptoms in this case

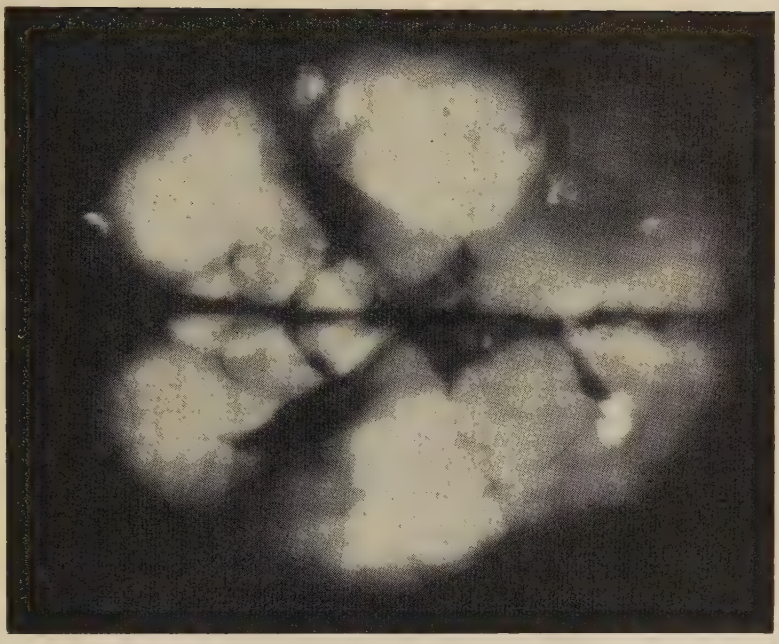

FIG. 3.—X-ray of brain after removal from another case of tuberose sclerosis showing diffuse distribution of the partially radio-opaque lesions.

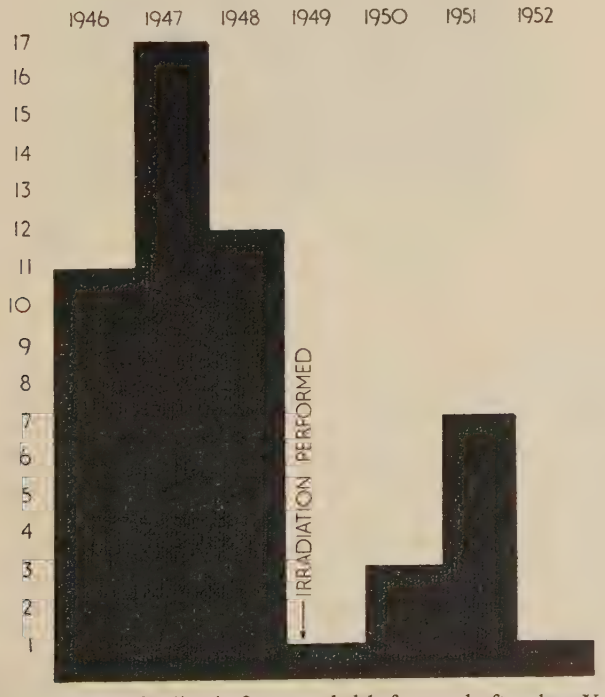

Diagram showing incidence of epileptic fits recorded before and after deep X-ray therapy to head in tuberose sclerosis.

particularly in 1947 suggests that one of the lesions had begun to spread, producing the additional right hemiplegia and other worsening of symptoms. It seems feasible that radiotherapy at this stage might have halted or even reversed the deterioration.

The pattern of the brain tumours differs sharply from that of many tumours and congenital abnormalities (Fig. 4). The more usual histological findings are

FIG. 4.—Patient D.J. showing very marked adiposity which developed after deep X-ray treatment at the time of puberty. Also note bilateral spastic diplegia with club feet. Photographed by Mr. J. E. Stevens.

described by Biggart (1949). These include a marked disturbance of the architecture of the brain and the presence of strikingly abnormal cells of uncertain origin and classification. In most of the nodules there is little evidence of active growth—a fact in keeping with clinical observations which suggest that only rarely does a particular mass acquire neoplastic properties. It is notoriously the sub-ependymal masses which do this. Potter (1952) illustrates one of these tumours. Even the more rapidly growing, highly cellular portions of tissue shown here have extremely diverse composition unlike that of a simple glioma.

Globus and Kuhlenbeck (1942) report a series of cases showing every degree of transition between tuberose sclerosis which they describe as "disseminated spongioneuroblastosis" and frank solitary tumours of the type of medulloblastoma. They consider that all these tumours arise from certain areas of the stratothalamic sub-ependyma which are rich in cell nests, notably the lamina terminalis. They demonstrate to their satisfaction by Nissl staining that at least

some of the giant cells both in tuberose sclerosis and in single tumours of this area are neuroblasts, hence the term neuroblastoma. All the tumours in this series were actively growing and rapidly fatal. In view of these facts no previous deduction about radiosensitivity seems possible and evidence on this point can only be obtained by experience. The very limited value of surgery in tuberose sclerosis (Kessel, 1949) and the difficulty of approach to tumours most of which arise from the strio-thalamic region is an additional reason in favour of more extensive trial of radiotherapy in appropriate cases.

Summary

A case of epiloia treated with deep X-ray therapy is reported. The number of fits has been conspicuously less since treatment but there is no improvement in the mental state or in the paralysis. It is suggested that a more extensive trial of deep X-ray therapy in epiloia should be made, especially in those cases beginning to show signs of deterioration. Possible radiosensitivity in the disease is discussed in relation to the morbid anatomy and histology.

Acknowledgments

My thanks are due to Dr. Frank Elliott for help and advice, to Dr. Doyne Bell under whose care the patient was at Charing Cross Hospital, to Dr. D. A. Pond for the electroencephalography, to Mr. L. Mushin for the eye examination, to Mrs. M. Marrs for the psychological reports and to Dr. L. Crome for the pathological material and for criticism.

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A COMPARATIVE STUDY OF RESULTS IN NEUROTIC PATIENTS TREATED BY TWO DIFFERENT METHODS

By

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In the outpatient department of the Maudsley Hospital, patients are seen in the first instance by members of the medical staff of consultant status at the diagnostic clinics, to which they are referred from a variety of sources, by far the greater number coming from general practitioners. From the diagnostic clinics there are several possible disposals, one of which is referral for outpatient treatment of a more prolonged and elaborate type, as opposed to treatment at a purely supportive level with brief interviews concerned with environmental factors and immediate practical problems. The more prolonged and elaborate outpatient treatment is under the supervision of a physician of consultant status with a Freudian analytical training and strong interest in psychotherapeutic methods. It is carried out by registrars under his guidance and may consist either of individual or group sessions, or of a mixture of the two, as he directs. His general outlook is well known (Foulkes, 1948). It has been a constant source of difficulty that the number of patients referred for this type of outpatient treatment has been greater than the resources of the hospital could manage, with the consequent development of long waiting lists and of the necessity for making awkward decisions with regard to priorities.

This state of affairs afforded an excellent opportunity for the investigation of the comparative efficacy of different therapeutic methods and it was decided that for a definite period all the patients referred for special outpatient treatment would be paired off and divided by the toss of a coin, half to be offered the usual psychotherapy and half to be offered the carbon dioxide treatment as recommended by Meduna. The period during which this was carried out was July, 1951 to March, 1952. During this time Dr. Foulkes, the physician in charge of the outpatient psychotherapy, agreed to accept all patients referred for psychotherapy. The patients had two more treatment interviews, one with the physician who recommended special outpatient treatment and one with the author at which they were told the type of treatment they were being offered, the coin having been tossed meanwhile, and at which the grading was done. Those whose first diagnostic interview happened to be with the author were graded at the time of the first interview and told their type of treatment by the therapist who was to carry it out.

All reports of the results of treatment in the psychoneuroses have encountered the same difficulty, namely that of assessment of the patients' condition. The subjective nature of the terms in common use, much improved, improved and so on, is self evident and needs no further elaboration, this being true even of such recent careful and painstaking publications as that of Miles,

Barabee and Finesinger (Miles *et al.*, 1951). For the purpose of this enquiry a method of grading dependent on social adaptation was employed which, although crude and liable to ignore small but substantial degrees of improvement, has the advantage of being readily understood and of conforming largely to the point of view of the general public. It had been found serviceable in a previous prognostic study (Harris, 1938). The four grades are as follows:

1. Unable to pursue their occupations on account of symptoms, and consequently an economic burden on their families or the community.
2. Able to work and earn a living, but forced by their symptoms to modify their lives considerably, resulting in much limitation of their interests and activities.
3. Able to lead full active lives, but at times seriously inconvenienced by symptoms.
4. Free from symptoms and apparently well.

The distinction between Grades I and II is usually very easy, the only difficulty arising in the case of housewives. Where someone else has to carry out the major part of their housewifely duties for them, however, I have put them in Grade I. The essential characteristic of Grade II is the restriction of activity by symptoms, inability to travel or to go out alone, fear of mixing with people leading to the dropping of healthy social contacts, fatigue necessitating excessive periods of rest or intolerance of crowds, closed spaces, cinemas and the like. Sometimes one had to evaluate such a symptom as occasional headaches, the consideration there being whether the patient regarded herself as ill and in need of treatment, in which case she was put in Grade III, or not, in which case she was put in Grade IV.

Out of a total of 120 patients 60 were put down for psychotherapy and 60 for carbon dioxide treatment. In the psychotherapy group 18, mainly on account of their unwillingness to co-operate but occasionally because of insuperable practical difficulties with regard to their work or family situations, never received any treatment at all and 4 had to be admitted to hospital, so that they must be regarded as failures from the outpatient treatment point of view. In the carbon dioxide group on the other hand 17 for similar reasons never received any treatment and 5 had to be admitted to hospital. There is therefore no substantial difference between the two groups as regards (*a*) the number of patients unwilling to accept treatment and (*b*) the number whose condition deteriorated so much that admission to hospital became necessary.

It is worth noting, however, that the patients did not know what kind of treatment they would be offered until they came to the preliminary grading interview with the author. All the seventeen patients who failed to receive treatment in the carbon dioxide group had seen the author and did know the details of the treatment proposed, but of the eighteen similar patients in the psychotherapy group six never came to the grading interview and so did not know what they were refusing. It seems pure chance that the six who did not come for their second preliminary interview were all in the psychotherapy group and this coincidence may obscure a tendency to refuse a treatment involving the inhalation of gas to a greater extent than one involving talking to a doctor. The impression was gained that more patients found the former unacceptable than the latter.

We are left with 38 patients in each group. It will be seen from Tables I and II that the two groups are very similar in regard to mental state, age, sex and duration of illness.

TABLE I

Age Group	Psychotherapy		CO_2	
	Female	Male	Female	Male
19–29	7	11	9	7
30–39	8	8	9	6
40–47	1	3	3	4
Marital State				
Married	13	13	18	8
Widowed	0	1	1	0
Single	3	8	2	9

TABLE II

Diagnosis	Psychotherapy	CO_2
Anxiety State	32	30
Obsessional Neurosis	3	3
Impotence	1	2
Depression	2	0
Hypochondriasis	0	2
Stammer	0	1
Grade at Onset		
I	8	4
II	14	14
III	16	20
Duration of Symptoms		
Under 2 years	13	14
Over 2 years	25	24

THE FOLLOW UP

The patients were all interviewed again by the author after an interval of between twelve to fifteen months, with the exception of three who were then living over 200 miles from London. These three all replied to a questionnaire and gave sufficient information by letter to enable them to be graded satisfactorily.

TABLE III

Grade at Follow up	Psychotherapy	CO_2
I	1	1
II	10	10
III	21	17
IV	6	10
Patients' View of Treatment		
Helpful	27	19
Unhelpful	8	16
Does not know	3	3
Changes during Year of Follow-up Period		
Remaining in I	1	1
From I to II	3	0
From I to III	3	1
From I to IV	1	2
Remaining in II	7	9
From II to III	7	3
From II to IV	0	2
Remaining in III	11	12
From III to IV	5	7
From III to II	0	1
i.e.		
Recovered	6	11
Improved	13	4
Unchanged	19	22
Worse	0	1

All the carbon dioxide group had finished their treatment, but 13 of the psychotherapy group were still attending for group or individual sessions. With regard to the relationship between the patients' opinions and the grading of those patients in the psychotherapy group who had improved or recovered, 15 thought the treatment helpful and 1 unhelpful; of those whose condition remained unchanged 12 thought the treatment helpful and 7 unhelpful. The corresponding figures for the carbon dioxide group were 7 and 5, and 12 and 11. The discordance is thus more marked in the carbon dioxide group. Some patients attributed their improvement to extraneous circumstances, such as the resolution of marital difficulties, often with good reason. Many of those who considered that they had been helped, although there had been no upgrading, reported minor alleviations of their condition, such as a reduction in the insistence or distressing quality of their symptoms.

Discussion

The figures show no significant differences between the two groups or a convincing superiority of one form of treatment over the other. Such differences as do exist indicate a trend in favour of psychotherapy, which the patients seem on the whole to appreciate as more helpful. It is clear, as was found in the previous investigation (Harris, 1938), that if one starts with a patient in Grade I it is much easier to secure substantial improvement. In other words getting the patient back to work is usually the easiest therapeutic task. The method does enable comparisons to be drawn between the progress of groups of neurotic patients. Use is made of social criteria of a fairly objective kind whose virtue is that they mean the same thing to different people and should not be affected by the idiosyncrasies of individual assessors. Such a procedure sheds no light on the indications for various treatments in neurotic illness and it is only made justifiable by the fact that these indications are at the present time so extremely ill-defined.

Summary

Hundred and twenty psychoneurotic patients were divided into two groups of sixty each and put down for treatment by two different methods, psychotherapy and carbon dioxide treatment. Their condition was assessed after an interval of a year. No really significant differences between the two groups were discovered. The methods employed were designed to eliminate subjective criteria as far as possible.

Acknowledgments

I am greatly indebted to my colleagues on the staff of the Maudsley Hospital, without whose wholehearted co-operation this investigation would not have been possible.

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CARBON DIOXIDE THERAPY OF THE NEUROSES

By

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(Received 8 January, 1954)

SINCE Meduna published his monograph on carbon dioxide therapy of nervous disorders (Meduna, 1950) the method has been widely employed. This paper discusses the results obtained by the strict application of the methods described by Meduna to 42 psychoneurotic out-patients at the Maudsley Hospital, and the bearing these results have on his claim that it is an effective and safe method of treating psychoneurosis, such as could be applied by practitioners with little psychiatric experience.

The patients were all seen first by consultant psychiatrists and selected as suitable for out-patient treatment. There were 18 men and 24 women. They are one-half of the patients discussed by Harris in his experiment which compares two forms of out-patient therapy (Harris, 1954).

The writer carried out most of the therapy, but Dr. D. Watt gave some of the earlier administrations. The patients breathed a mixture of 30 per cent. CO_2 and 70 per cent. oxygen from a mask until they were unconscious; this required from 20 to 50 breaths, but the number tended to be the same for any one patient. We counted the breaths aloud, and afterwards asked the last number remembered; a clear gap showed unconsciousness had been reached.

We found Meduna's descriptions accurate and saw much that he describes; autonomic reactions, flushing and sweating; muscular twitchings and jerkings, passing to opisthotonic spasms; emotional "abreactions" with weeping, crying and outbursts of violence. No comment was made to the patients about any of these, nor was any enquiry made about their sensations or the content of their dreams. We refrained from all exhortation or suggestion, discussing as few details as possible with our patients. We told them this was a new form of treatment about which there were favourable reports; that they would take a number of breaths from the mask and then become unconscious. We said that the experience was similar to "gas at the dentist's" and the dangers comparable. We administered the gas as far as possible three times weekly and about once a fortnight enquired how the symptoms were. If the patient spoke of stopping treatment we would encourage them to continue if they had had only a few administrations, but if they had had more than twenty without any change we readily let them cease, as Meduna advises. At various stages a number refused to carry on or stopped coming to the clinic.

The "abreactions" varied greatly from patient to patient and from session to session. Some patients never showed any disturbance. Others reacted violently, some women screaming and struggling with the nurses. A few patients showed movements that seemed sexual—thigh rubbing, back arching—while one (see below, Case 4) had orgastic spasms. Histrionic individuals tended to produce more violent demonstrations, but the liveliness and frequency of the reactions bore no relation to the therapeutic result.

Results

Three assessments of the patient's progress were available. At the end of the course of administrations a note was made whether the symptoms seemed better, worse, or the same. About six months after the end of treatment an independent assessor (Dr. A. Harris) saw the patients, measured their degree of disability and compared it with their state before treatment. The follow-up took place twelve months after the original interview and referral for treatment; in most cases the follow-up interview occurred more than six months after the end of treatment, but in a few where the treatment was protracted the gap was less. After discussion of their present state the patients were asked whether they had found the treatment helpful or unhelpful. To state the results of treatment, these three assessments were combined, the patients falling into four categories:

A. *Improved:* Those patients who felt they had been helped and who showed improvement in their degree of disability at the follow-up.

Case 1. A housewife of 30 had suffered from periods of depression, constant tension and anxiety, and psychosomatic symptoms, especially indigestion, for 6 years; there had been no periods of relief, and the symptoms had been increasing steadily during the past year. She had 17 administrations between 2.v.52 and 25.vi.52, requiring 40-50 respirations, without any marked emotional excitements. She disliked the administrations, but improved steadily. At follow-up on 15.iv.53 she felt better than she had been for years; her periods of depression had ceased, and her indigestion was negligible, recurring only in anxiety-producing situations. Her disability was much less; she was doing more and was no longer hampered in her daily life by her symptoms. She had no doubt the treatment had done her a great deal of good.

B. *Helped:* Those patients who had seemed improved at the end of treatment and who said it had helped them, but whose disability showed no rateable change.

Case 2. An unmarried bank clerk of 25, complained of self-consciousness, blushing and trembling of the hands, especially in social situations, which had increased over the last 4 years. He had 31 administrations between 16.iv.52 and 27.vi.52 requiring 40-45 respirations; he usually showed a stereotyped stretching of his arms during unconsciousness, but had no emotional reactions. At the end of the course he reported that he felt a marked improvement which had started quite suddenly after the fifteenth session; he admitted that he did not like the administrations. At follow-up on 20.i.53 he still felt that the treatment had helped him and that he was improved. He still had some social anxiety, but it was less, and he had now a regular friendship with a girl, something he had never managed before. The rating of his disability, however, showed no change.

C. *Unchanged:* Apart from those who declared and showed no change, this category includes two other groups:

(1) Seven patients who stated that the treatment was unhelpful, but who showed an improvement in their disability; investigation showed that this improvement was due to other factors operating within the twelve months, e.g. a separation from an incompatible husband, effective contraceptive measures, a marital reconciliation.

(2) Two patients who were in a worse state at the end of twelve months (one worse on the objective rating, the other admitted to hospital) but in whom this did not appear to be connected with the CO_2 therapy.

Case 3. An unmarried bank clerk of 32 complained of feelings of depression and inadequacy over many years and inability to make contact with women or face social situations. He had completed satisfactorily a secondary education and six years' active service in the Army, but since 1946 he had been increasingly depressed by his inadequacy and had sought psychiatric treatment at several hospitals ; he had attended a social club, had had 6 months' psychotherapy, and had been an in-patient in a Rehabilitation Centre for 10 weeks, where he had had 1 E.C.T. He had 4 administrations of CO_2 between 18.iv.52 and 25.iv.52, unconsciousness being achieved during the latter two. He did not attend again but wrote saying that since the treatment gave him headaches and made him vomit he did not wish for any more. At follow-up on 15.xii.52 his condition was unchanged. He said that the CO_2 had not been helpful, and that he had since been to several other hospitals, had been for 3 weeks an in-patient in a mental hospital where leucotomy was suggested, and was now having acetyl-choline injections as an out-patient.

D. *Worse:* Includes those patients who had to be admitted to hospital during or immediately after their CO_2 administrations, or who were made worse by the treatment, and on reflection later still felt it had been unhelpful.

Case 4. An unmarried woman of 32 complained of lassitude, dyspepsia, and difficulties in social relationships. She had had a disturbed unhappy childhood and lifelong personal difficulties; despite good intelligence and an adequate education she had failed in various careers, including nursing; she had had several close women friends, but had always shown a marked dislike of men. She had 18 administrations between 18.iv.52 and 15.vi.52. She always showed a marked reaction, and on 5 occasions exhibited body arching and thigh flexing of an unmistakably sexual nature. On recovery she usually wept bitterly, but expressed a desire to carry on with the treatment, claiming that she was better. Two days after her 18th administration, however, she had to be admitted to hospital in a dissociated state which rapidly developed into a state of terror and hallucinations, during which she heard voices accusing her of being a sex maniac and a beast. This state has persisted with brief intermissions for over a year, with only transient improvements after a course of electro-convulsive therapy and later a planned psycho-therapeutic approach over 2 months; she remains a patient in a disturbed ward and in April, 1953 was being considered for leucotomy. In her clearer periods she says she has no doubt that the carbon dioxide treatment made her worse.

The numbers in these 4 categories were:

Improved	8 patients
Helped	12 patients
Unchanged	13 patients
Worse	9 patients

To give the usual categories, the first two can be combined. We then have "Improved" 20 patients (48 per cent.), Unchanged 13 (31 per cent.), and Worse 9 (21 per cent.). These are unexceptional figures, such as may emerge from any method of treating psychoneurotic disorders. They certainly do not warrant any striking claims.

Some of the patients gave up after a very few treatments. Thirteen patients had less than five administrations; of these 1 was helped, 8 were unchanged, and 4 worse. Five patients had between five and ten administrations; of these 2 were improved, 1 helped, and 2 worse. If we discard all patients who had less than ten administrations, the general figures are 6 improved, 10 helped, 5 the same, and 3 worse.

Thirty-five of the patients were diagnosed as "anxiety state" at the original consultation. Four patients were classified as obsessive-compulsive neurosis; they had 2, 6, 12, and 20 administrations. The first three were made worse by the treatment, while the last one is classified as unchanged; all four felt the treatment had been unhelpful and had frightened and upset them. Meduna noted in his monograph that not one of eleven patients with obsessive-compulsive illnesses treated with CO_2 received any benefit, but does not comment further on this. Other special diagnoses were impotence (2 patients, 1 improved, 1 unchanged), and one stammerer who was improved.

Therefore, if we exclude the obsessionals (4) as Meduna would suggest and disregard all of the others that had less than ten treatments (16), we are left with 22 patients of whom 16 were improved to some degree, i.e. 73 per cent. This figure is more in line with those of the more enthusiastic writers on this therapy.

Discussion

There have been several reports on carbon dioxide therapy for the neuroses with variations on the method Meduna describes (Milligan, 1951; Silver, 1951; Peterson, 1952). Two pilot studies have been reported, using Meduna's method. Weaver, Peterson, and Anderson treated 13 in-patients with varying frequencies of CO_2 but without added psychotherapy; nine of these patients showed improvement, while 4 showed no change (Weaver *et al.*, 1951). Baars treated 12 out-patients. Of these twelve, five refused after the first few sessions and two others showed no change, but five showed differing degrees of improvement (Baars, 1951).

There have been four major studies of carbon dioxide therapy with numbers greater than ours.

Meduna's monograph reports on the results in 100 patients of whom 68 were improved, but they are rather difficult to assess, since he reorganizes the patients according to a new classification of psychoneurotic disorders which excludes obsessive compulsive states and includes patients with stammering or impotence. Of his 100 cases, 33 were stammerers, 21 sufferers from character neurosis or inferiority neurosis, and 10 from homosexuality or alcoholism. It is with these patients, especially the stammerers, that he reports the best results. Only 8 patients are classified as anxiety states, and of those, four were improved two unchanged, and two were worse and required insulin or electroshock.

Jackmann and Schorr, working in conjunction with Meduna, report most favourably. They are more interested in the mode of action of the treatment than proving its therapeutic success, but they do mention the results with ten new patients. One was unchanged, one slightly improved, and eight were improved greatly. Jackmann states that this proportion is typical of his experience with another 90 patients during recent years (Jackmann and Schorr, 1952).

Kindwall reported on the treatment of in-patients. He had treated over 100, though only 37 are analysed in detail. Many of these patients had psychotherapy at the same time. Of the 37, 18 recovered, 11 were unchanged, and 8 were worse. This total includes 4 obsessionals, of whom one was recovered, 1 unchanged, and 2 worse (Kindwall, 1949).

Moriarty reported on treatment of private patients with CO_2 and psychotherapy. He had treated some 213 patients but examined only his first 66. He found the treatment ineffective in major psychoses and established obsessive-compulsive states. Of his 66 cases, 26 were much improved, 28 improved, and 12 unimproved (Moriarty, 1952).

Our results tally with these in certain respects. Patients with obsessive-compulsive neurosis are not helped by carbon dioxide therapy. It appears to have helped patients who had been resistant to other forms of therapy. In those series that are carefully reported there seems to be a considerable number of patients who fail after the first few treatments, some being so upset that they do not wish for any more. Of those that stay, a high proportion are improved. If those who lapse or refuse are counted in, the total figures are not very impressive —only about half the patients are improved; if, however, these early refusals are not counted, figures of 70-80 per cent. improvement result.

The administration of CO_2 appears to be remarkably free from physical risk. The papers examined cover some 20,000 administrations; the only report of untoward effects is that of Meduna (p. 41), who mentions the development of widespread subcutaneous petechial haemorrhages over the head and shoulders of a severe chronic alcoholic during his third treatment—without lasting ill effects. Sargant reported a circulatory collapse of some hours, but the patient had not only had a very deep CO_2 anaesthesia but a heavy dose of intravenous thiopentone beforehand, which may have been the cause; again there was no lasting ill effect (Sargant, 1953, personal communication). There is, however, a risk of ill effects on the mental condition. Kindwall reports patients made worse. Moriarty speaks of severe anxiety or depression being aroused, and Meduna, both in his monograph and in a discussion of Moriarty's paper, mentions the dangers of the acute anxiety which may be stirred up. Our cases (especially Case 4) confirm this. Carbon dioxide therapy is not safe for widespread use by those without psychiatric experience. It cannot be applied mechanically, and the patient's progress must be carefully watched.

Meduna claimed that carbon dioxide therapy was of great benefit in treating psychoneurotic patients, often producing beneficial change in people who had had many other therapies previously; he said that it did not benefit psychotic or obsessive compulsive states, and admitted that some patients were made worse. Our series confirms much of this but suggests that the proportion of improved patients is not as high as has been stated if the patients who cease treatment during the first few sessions are counted; it further suggests that the deleterious effects may be more frequent and more grave than has been indicated.

There have been few attempts to explain why the therapy should produce these results. Meduna adduces many neurophysiological facts which he links with McCulloch's theories of reverberating circuits, but he does not explain why obsessive-compulsive neuroses are consistently made worse. Jackmann likens the results to those of leucotomy. Freeman discusses the psycho-dynamic significance of the experience of being gassed and intensely excited, also the unconscious phantasies this may activate (Freemann, 1952). Some of my observations, for example the content of the subsequent hallucinations of Case 4, suggested that such mechanisms do operate, though it is impossible to say how great their role in producing change may be.

Summary

Forty-two psychoneurotic out-patients were treated by Meduna's carbon dioxide narcosis therapy; his method was followed strictly. Twenty patients were improved, 13 unchanged, and 9 made worse. These results are analysed and illustrative cases described. The results are compared with those of other workers.

Carbon dioxide therapy is physically safe but must be carefully controlled as it may lead to psychotic breakdown. It usually makes obsessional states worse. Some patients with anxiety states cease treatment, but those that remain mostly do well.

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CLINICAL SIGNS, DIAGNOSIS AND PROGNOSIS IN THE FUNCTIONAL PSYCHOSES

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In a previous enquiry the prognostic significance of diverse aspects of the functional psychoses was examined (Harris and Lubin, 1952; Harris and Norris, in press). Prognosis was evaluated in terms of total length of stay in a mental hospital over a follow-up period of 18 years. Each patient was assigned to one of three major diagnostic groups (schizophrenia, affective psychosis or atypical psychosis), the diagnosis being based on Kraepelinian and Bleulerian criteria. The diagnosis was made by one of the authors (A.H.) on the evidence of 20-year-old case notes written by a large number of different psychiatrists. In this investigation the same author himself examined all the patients included in the series. We felt it would be interesting to compare the predictive value of diagnoses made by the rough and ready method of the earlier survey with that of those made by a detailed examination of the patients concerned, as in the present survey. For reasons previously stated (Harris and Norris, 1954) we feel that only certified patients admitted in the second period are comparable with the types of cases admitted in 1930. If a diagnosis of schizophrenia is held to connote an unfavourable and the remaining categories a favourable outcome then in the first series 60 per cent. of the patients were correctly classified while in the second series 58 per cent. of the certified patients were assigned to their correct diagnostic group. This difference is not significant. Thus it would appear that a more sophisticated application of Bleulerian methods of diagnosis does not necessarily give rise to more reliable evaluation of prognosis. Accordingly we have attempted to dissect these three diagnostic categories to determine whether any of the components show prognostic significance. For this purpose we took the second series because for these patients there were available detailed clinical descriptions made by one of the authors (A.H.) in the observation ward of a general hospital, prior to the patient's transfer to a mental hospital. Unfortunately 13 of the case notes containing these detailed clinical descriptions had been lost, so that we could only use 187 patients out of the total of 200. They were first admitted to hospital in the period May, 1940 to May, 1942 and were followed-up for the next 10 years. The result of the analysis is set out in the table.

Very few attempts have been made so far to assess the prognostic value of simple clinical signs, most workers having devoted their attention to broad and

comparatively ill defined categories. Skottowe has stressed the gravity of dyssymbole, a disturbance apparently closely allied to, if not identical with, Bleuler's thought disorder, more especially with regard to the likelihood of the patient responding to shock therapy (Skottowe, 1939). Albee has investigated the effect of different types of delusions in schizophrenic patients from this standpoint, concluding that self-reproachful delusions were on the whole of favourable import and persecutory delusions of unfavourable (Albee, 1951). Langfeldt has emphasized the seriousness of delusions of influence which he regards as the "process" symptoms par excellence (Langfeldt, 1939).

In this work we have arbitrarily defined three prognostic ratings as follows:

Favourable Shown as *F* in text. Patient spent a total period of less than 3 years in hospital and was alive at the end of our 10 year follow-up period.

Intermediate Shown as *I* in text. Patient was in hospital for periods totalling 3 to 9 years and alive at end of follow-up, *or* patient died in hospital within 5 years of admission.

Unfavourable Shown as *U* in text. Patient was in hospital for 9 or more years and was alive at end of follow-up, *or* patient died after spending more than 5 years in hospital.

The figures in the table point strongly to the prognostic significance of the patients' affective state. In the series as a whole 52 per cent. of the patients were in group F, 12 per cent. in I and 33 per cent. in U prognostic groups. Among patients showing consistent depression or elation 77 per cent. were in F, 12 per cent. in I and 11 per cent. in U outcome group. Conversely 21 per cent. and 66 per cent. of patients with shallow or inappropriate affect were in the F and U groups respectively. It is clear that estimation of the patients' affective state has played a great part, if not the major part, in the process of diagnosis. All affectives show some mood disturbance, flatness or inappropriateness of affect is usually associated with a diagnosis of schizophrenia, although schizophrenics frequently show no disturbance of mood, and atypical cases show no association with any particular mood disturbance. These associations of diverse moods with different diagnoses are highly significant (Chi Square$=146$; d.f.$=6$; $P<\cdot0001$). Thus although the differences in outcome in relation to mood disturbances are also highly significant (Chi Square>28; d.f.$=6$; $P<\cdot0001$) the main effect is to confirm the previous findings concerning the predictive importance of diagnosis. However in view of the lack of uniformity shown by individual psychiatrists and clinics in their diagnostic habits these results are not without interest and may point the way to clearer cut diagnostic criteria.

In the schizophrenic group alone 35 per cent. were in F, 15 per cent. in I and 50 per cent. in U. Among 5 showing consistent elation 4 were in F outcome group and among 50 with shallow or inappropriate affect 33 were in U group. To get statistically significant differences we must compare schizophrenics who present shallow or inappropriate affect with those who do not, when it appears that shallow or inappropriate affect is associated with a bad prognosis (Chi Square$=10$; d.f.$=2$; $P<\cdot01$).

Clusters of signs in association with the main disturbances of mood occur much as might be expected. Agitation was closely linked to depression, only two patients in fact being consistently agitated without also being consistently depressed. Of the patients who showed inappropriate laughing, grinning and/or giggling only one was not noted to show shallow or inappropriate mood also,

Symptomatology of the Three Diagnostic and Prognostic Groups

	Diagnosis						Prognosis					
	Schizophrenia		Affective		Atypical		Favourable		Intermediate		Unfavourable	
	No.*	Per cent.	No.*	Per cent.	No.*	Per cent.	No.*	Per cent.	No.*	Per cent.	No.*	Per cent.
Total Number of Patients	98		49		40		98		28		61	
Disturbance of mood												
1. Consistent depression	4	4·1	41	83·7	9	22·5	42	42·9	7	25·0	5	8·2
2. Consistent elation	2	2·0	6	12·2	4	10·0	9	9·2	1	3·6	2	3·3
3. Consistent agitation	1	1·0	20	40·8	4	10·0	20	20·4	2	7·1	5	8·2
4. Deteriorated mood	49	50·0	—	—	3	7·5	11	11·2	7	25·0	34	55·7
5. Other	7	7·1	2	4·1	11	27·5	13	13·3	2	7·1	7	11·5
6. No disturbance of mood	35	35·7	—	—	12	30·0	25	25·5	9	32·1	12	20·0
Disturbances of thought												
7. Thought disorder	48	49·0	—	—	7	17·5	27	27·6	9	32·1	22	36·1
8. Flight of ideas	—	—	6	12·2	1	2·5	7	7·1	—	—	—	—
9. Retardation	1	1·0	3	6·1	—	—	3	3·1	—	—	1	1·6
10. No disturbance of thought	48	49·0	40	81·6	31	77·5	61	62·2	19	67·8	36	59·0
Disturbances of behaviour												
11. Inappropriate laughing, grinning and/or giggling	21	21·4	—	—	1	2·5	3	3·1	5	17·8	14	22·9
12. Bizarre mannerisms, postures and/or grimaces	21	21·4	—	—	1	2·5	8	8·2	1	3·6	13	21·3
13. Bizarre impulsive outbursts	9	9·2	—	—	4	10·0	5	5·1	2	7·1	5	8·2
14. Negativism	4	4·1	—	—	—	—	1	1·0	2	7·1	1	1·6
15. Suicidal attempts	1	1·0	11	22·4	1	2·5	10	10·2	3	10·7	1	1·6
16. Other disturbances of behaviour	—	—	1	2·0	3	7·5	5	5·1	1	3·6	1	1·6
17. No disturbances of behaviour	49	50·0	38	77·5	29	72·5	67	68·4	17	60·7	30	49·2
Hallucinations												
18. Auditory	49	50·0	3	6·1	12	30·0	20	20·4	12	42·8	32	52·4
19. Visual	8	8·2	—	—	4	10·0	6	6·1	3	10·7	4	6·5
20. Other	2	2·0	1	2·0	—	—	—	—	1	3·6	2	3·3
21. None	47	48·0	45	91·8	26	65·0	77	78·6	15	53·6	27	44·2
Delusions												
22. Of influence	10	10·2	—	—	1	2·5	6	6·1	2	7·1	3	4·9
23. Persecutory	31	31·6	2	4·0	13	32·5	16	16·3	12	42·8	18	29·5
24. Grandiose	12	12·2	4	8·2	3	7·5	9	9·2	3	10·7	4	4·5
25. Hypochondriacal	8	8·2	12	24·5	5	12·5	16	16·3	5	17·9	5	8·2
26. Of guilt	—	—	15	30·6	6	15·0	17	17·3	4	14·3	3	4·9
27. Of impending disaster	—	—	6	12·2	1	2·5	6	6·1	—	—	1	1·6
28. None	45	45·9	18	36·7	16	40·0	40	40·8	8	28·6	30	49·2

* Some patients exhibited more than one phenomenon in each group and have been counted more than once. For example 18 patients with affective psychosis had no delusions (49—18)=31 patients had at least one delusion and of these 8 had more than one so that the total number of delusions presented was 39, i.e. 36·7 per cent. patients had no delusions and (100—36·7) per cent.=64·3 per cent. had at least one.

of the patients who made suicidal attempts only one was not consistently depressed and of those suffering from delusions of guilt only four were not consistently depressed. This suggests the most likely explanation of Albee's findings, namely the association of self-reproachful delusions with depressed mood and the possibility that rather different diagnostic criteria from ours were applied to his patients.

Signs not associated with a particular mood change, such as disturbances of thought and behaviour and the presence of various types of hallucinations and delusions, did not seem to affect prognosis.

Shallow or inappropriate affect is not a sign of longstanding illness in our series. Of the 52 patients who showed it, the time between first appearance of symptoms and examination of the patient on first hospitalization was under 6 months in 23, 6-12 months in 5, 12-24 months in 7, over 24 months in 9 and unknown in 8. There was no significant excess of patients with shallow or inappropriate affect in the 30 to 40 age group (Chi Square <6; d.f.$=2$; $P>\cdot05$). Similarly other disturbances of thought and behaviour, hallucinations and delusions did not vary significantly in their incidence in the 3 age groups, under 20 years, 20 to 30 years and 30 to 40 years. The general effect of age was somewhat similar to that found in the previous series, there being a statistically significant excess of patients under 20 in the F group and of patients over 30 in the U group (Chi Square$=23$; d.f.$=4$; $P<\cdot001$).

Discussion

Flat or inappropriate affect emerges as the most definite indicator of a bad prognosis, a finding which is not novel or unexpected since it has in the past frequently been regarded as a sign of long-standing illness and chronicity. However, this series of patients shows that it may appear early in the disease and still be of grave import. It is noteworthy that this finding emerges clearly in spite of the limitations of the investigation, namely, the smallness of the sample, the crudity of the prognostic criteria and the fact that the patients were examined and data collected by a busy clinician who at that time did not envisage the present enquiry. It is common knowledge that the so-called schizophrenic residual state consists largely of this affective change and that it frequently does not prevent patients living out of hospital. If a more detailed follow-up were undertaken and more precise observations on the affective state in the early stages of the illness made the results might be even more striking. In the latter connection accessory methods of examination might usefully be employed. For example, Grauer, using a modification of the Rorschach, obtained results much in line with ours (Grauer, 1953).

One has the impression that psychiatrists would agree more readily on the presence or absence of this affective change than they would on the diagnosis of schizophrenia, but the real nature of the disturbance remains obscure. One of us observed that chronic schizophrenic patients were capable of strong affective responses, but that the necessary stimulus is quite different from that which would be effective in normal people (Harris, 1938) and recent experimental work has confirmed this (Malmo, Shagass and Smith, 1951). Perhaps the underlying defect is in motivation, as Kraepelin seems to have thought according to his concept of *Willenstörungen* and some recent experimental work suggests (Pascal and Swenson, 1952). Whether affective shallowness or incongruity is a specific qualitative change or merely a phenomenon which appears when a certain stage of mental disintegration has been reached is quite unknown.

Summary

A group of 187 patients suffering from functional psychoses whose first hospital admission occurred before the age of 40 and who were examined on that first admission by one of the authors were followed-up for a period of 10 years. The predictive value of the diagnosis made at the onset of the illness with regard to length of hospital stay was compared with that in a previously published series where the diagnosis was made under apparently less satisfactory conditions. No differences between the two series in this respect were found. An analysis was then made of the most prominent individual clinical features in the patient's mental states with a view to assessing (1) the part that they had played in making a diagnosis, (2) their prognostic value. The results point to the affective state as the most significant finding both with respect to prognosis and diagnosis. Thought disturbances, hallucinations and delusions unassociated with mood changes had no prognostic significance. Flatness or incongruity of affect emerged as the most definite indicator of an unfavourable outcome.

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THE MEASUREMENT AND DESCRIPTION OF SPONTANEOUS MOVEMENTS BEFORE AND AFTER LEUCOTOMY

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Most spontaneous movements are considered to be motor expressions of the feelings and emotions (Stagner, 1948). Many movements of this kind are referred to as "nervous" habits or mannerisms, a description in which this assumption is also implicit. It is surprising, therefore, that so readily available and objective a guide to the affective organization of the personality has been studied relatively little: the difficulties of definition, description and measurement may account for this. Olson (1929), however, devised a useful time-sampling technique for measuring nervous habits, but I know of no investigations in which it has been used to compare the spontaneous movements made by healthy and "nervous" subjects.

The present investigation aimed at finding a satisfactory method of measuring spontaneous movements in patients with mental illness, and then studying some of the psychological and physiological factors affecting them. Patients who had been subjected to leucotomy seemed a suitable group for such a study because their movements can be compared, not only with those of healthy controls, but also with their own before operation. In addition the leucotomy provided an opportunity to enquire into the function of the pre-frontal areas in determining this sort of psychomotor activity.

In order to state the main problem more clearly, it is necessary to define the movements being investigated. Under spontaneous movements I include all involuntary movements believed to be related to mental processes (gestures, hyperactivity, tics, etc.); involuntary here signifies "unrelated to any consciously recognized purpose which such movements could bring about". The great majority are expressive movements and may be divided into two principal categories:

Autistic Gestures

Krout (1935) described the apparently meaningless, self-directed, often repetitive fidgetings, so common in states of preoccupation, as autistic gestures; for he was able to show that they are a form of self-communication the purpose of which is a partial or substitute expression of an inhibited motor-activity. Krout listed 340 of them: adjusting tie, biting nails, tapping fingers are examples. Olson (1929) also made an inventory of movements of this kind, but called them nervous habits. If, as is commonly believed, they are an expression of an emotional state or represent, as Krout suggests, another inhibited activity, they might be more prominent in mentally ill patients than in healthy subjects; and therapy, such as leucotomy, if successful, might decrease their frequency.

Communicative Gestures

In contrast to the above, these gestures often accompany speech and serve a social purpose, that of communication. A large proportion of them are movements of the hands and face employed for emphasis and for the expression of emotion. If communicative gestures are conceded to be more numerous in anxiety, then their number might be expected to diminish following a successful leucotomy operation in which agitation and anxiety are relieved; but if, as the studies of Petrie (1949) and Crown (1953) suggest, patients tend to be more extravert after the operation, a relative increase of communicative (social) over autistic (self-directed) gestures might be predicted.

Experimental work in animals bearing on the subsidiary problem, the function of pre-frontal areas in determining spontaneous movements, was reviewed by Reed (1947). Frontal lesions commonly increased spontaneous movements. Monkeys, however, become restless only when the cut isolates area 13 (Ruch *et al.*, 1943; Freudenberg *et al.*, 1950). Diminished activity has been observed in patients who have had a standard leucotomy or an operation limited to areas 9 and 10 (Freeman *et al.*, 1939; Pool *et al.*, 1949), but an increase is often reported when the cut isolates the orbital gyrus, especially its ventromedial part (Reitman, 1946; Egan, 1949; Fulton, 1951). Kinder *et al.* (1952) attempted to measure "general activity and social behaviour" by a more objective means than clinical reports. They obtained scores of the patients "gross activities" (movements about the room, attention to objects and self-directed movements) by using a time-sampling procedure. They observed a patient alone before and after leucotomy, and again in the presence of a second patient when scores of both patients' social activity were also obtained (verbal and communicative movements). The results were inconclusive: a tendency for the younger patients to increase activity, and for the older to decrease activity following operation was claimed.

The principal objects of the following experiments were: first, to investigate the validity and reliability of a new method of measuring spontaneous movements; and secondly to test the hypothesis that spontaneous movements increase with emotion by comparing movements in anxious, tense patients awaiting leucotomy, (*a*) with those in healthy controls, and (*b*) with those in the same patients after leucotomy. Two further observations were planned. It was hoped that: (*a*) by relating the anatomical area of the leucotomy cuts to changes in movement that differences in effects of the different areas might be recorded; (*b*) by recording the character of the patients' gestures, changes following the operation might be observed; a tendency to more extroverted expressive movements was postulated.

Method

Apparatus

The number of movements made by a subject was measured with an electromyograph (E.M.G.) which included an electronic integrating circuit. There were two channels, so that the activity in two separate muscle groups could be counted.

Surface electrodes were used. They were silver cups, 1 cm. in diameter, filled with electrode jelly. In each channel the action potentials were fed to a pre-amplifier and then to an integrating circuit which operated an electromagnetic counter. The potentials were also fed to an oscilloscope and to a teledeltos pen recorder so that all activity picked up could be monitored and artifacts avoided. Calibration tests had shown that the counts varied with the

input voltage (frequency constant), and therefore with the amplitude of the muscle potentials. Similarly, the counts varied directly with frequency (voltage constant), and so with the repetition rate of the muscle potentials. It may be assumed, consequently, that the counts obtained on each channel were proportional to the total activity occurring in the motor units underlying the electrodes. A setting of the gain of the pre-amplifier was found at which the larger potentials which accompany a movement would operate the integrating circuit, while lesser activity, such as that of reflex postural tone, did not do so.

Procedure

The patient sat at a card table which was placed close to him so that leg movements were prevented and trunk-movements discouraged. This arrangement was intended to promote movements of the arms and wrists. It was decided to measure the latter because they are essential to a large majority of autistic gestures, e.g. manipulations of the face, mouth, fingers, body and table top. All the nervous habits included by Olson (1929) in his condensed inventory, except facial grimacing, tongue protruding and blinking, necessitate hand-movements; as also do 60 per cent. of the gestures in Krout's (1935) comprehensive list.

The electrodes were fixed by adhesive plaster over the crests of the forearm extensors of the right and left arms. Light, unobtrusive leads passed to the back of the chair, and from there to the E.M.G. which was screened from the patient.

Before beginning the recording the patient was encouraged to move freely and to forget the electrodes by asking him to smoke or to turn the pages of a magazine for 10 minutes. It was found that he quickly became accustomed to, and apparently unaware of, them. The experimenter then left the patient alone and unoccupied for 10 minutes, circumstances which favour the appearance of autistic gestures. The counts obtained every minute from the right and from the left arm were added and the mean score for the period computed. This provided the autistic score.

At the end of the first 10 minutes alone the patient was interviewed for 10 to 15 minutes. He would, as a rule, accompany his conversation with communicative gestures. Some patients, however, persisted in autistic activities also, but the communicative gestures predominated, the mean count recorded per minute of interview was taken to be the communicative gesture score.

The session ended with another period alone to obtain data for measuring the reliability of the autistic movement score.

Where possible these sessions were repeated twice before operation, and also following it at 3, 6, and 12 months. Not every patient was able to attend the full number of sessions.

Motion pictures of the patients' movements and facial expression were taken before and after leucotomy. Their purpose was: first, to check on the validity of the electromyographic measurement of movements; secondly, to assess changes in the character of spontaneous movements following leucotomy; and thirdly to obtain an objective rating of the patient's manifest anxiety and tension (facial expression and psychomotor activity were each rated on a three point scale). The last ratings were combined with a rating (on a five point scale) of the patient's report of his feelings to give a tension and anxiety score for each patient.

Validity of the E.M.G. Method

This was assessed by concurrently watching the patient's movements, the activity on the oscilloscopes, and the counters. A satisfactory correspondence

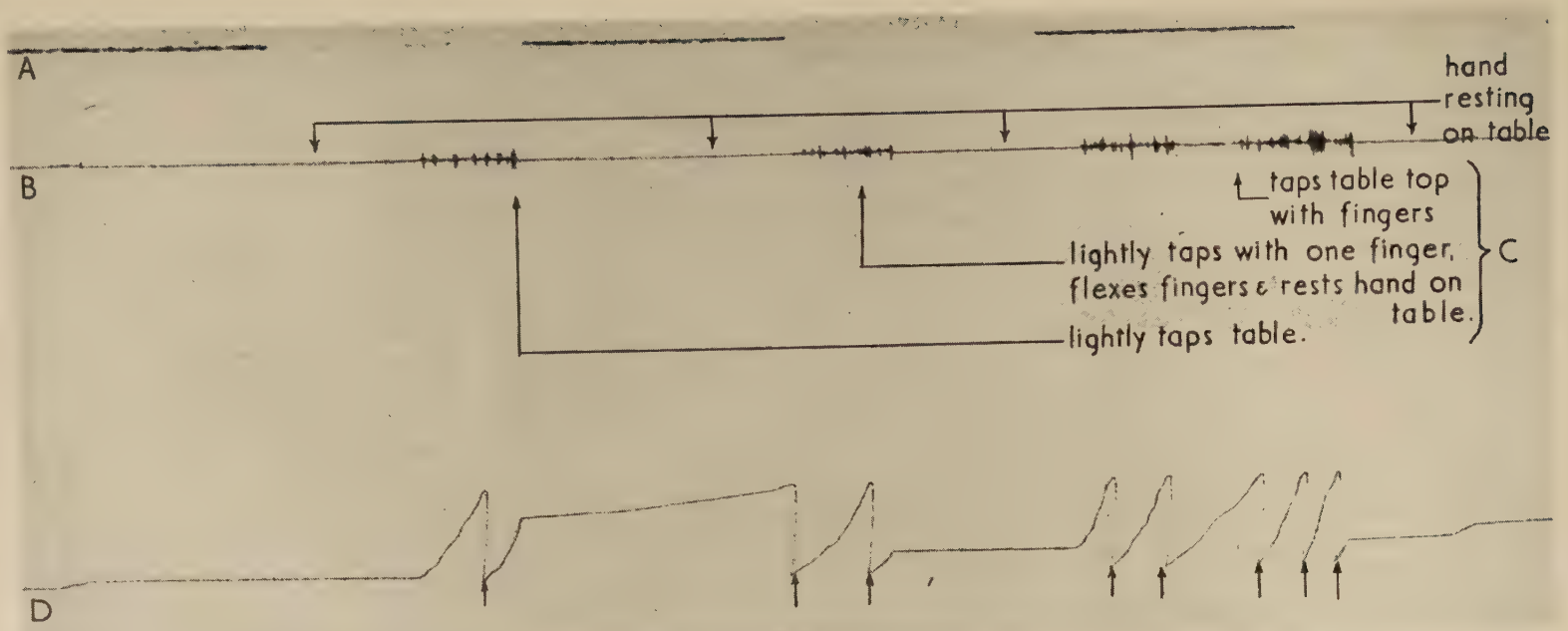

FIG. 1.—Shows a record of movements made by a patient during 60 seconds and the muscle potentials recorded and counted in his R. forearm.

A—Time marker—10 second intervals.

B—Pen recording action potentials from R. forearm extensors.

C—Gestures observed.

D—Counts recorded from R. forearm extensors.

was found between movements observed and action potentials both observed and counted. Figure 1 illustrates these points. It shows one minute of a typical tracing of the action potentials and counts from the right forearm. On this occasion, in order to demonstrate the relations between the action potential tracing and the counts they give rise to, both channels are recording from the right forearm: the pen on channel 1 is tracing the action potentials directly, that on channel 2 is being fed through the integrator and is marking the summed action potentials.

The patient's movements when alone were seen to be nearly all of the kind listed by Krout (1935) as autistic gestures; but if, as occasionally happened, he made movements of a more voluntary, "adaptive character", such as putting his hand in his pocket to take out his watch, then the counts for that minute were discarded. Finally, the patient's position was, in fact, found to foster movements of the sort which necessitated wrist and hand movements and, therefore, activity of the forearm extensors.

To procure a statistical measure of the validity of the E.M.G. scores, motion pictures were taken of movements made by normal subjects sitting alone and a time-sample score of the filmed movements obtained; these were then correlated with the E.M.G. scores of movements recorded concurrently. The method of scoring spontaneous movements by means of motion pictures is described elsewhere (Sainsbury, 1954). The correlation (r) between the time-sampled movement scores from 20 films of healthy male subjects and the movement scores they obtained on the E.M.G. was 0·87. From this it was concluded that the E.M.G. gave a valid measure of the subject's spontaneous movements.

The Reliability of E.M.G. Measures of Spontaneous Movements

The scores of spontaneous movements obtained during the first and second periods alone of 26 sessions were correlated to give a test-retest measure of reliability. The product-moment correlation was $0 \cdot 834 \pm 0 \cdot 040$. The E.M.G. measures, therefore, had a good reliability. It also follows from this finding that the number of movements made by any patient tended to remain at a level characteristic of him.

The Subjects

Ten patients previously selected for leucotomy were investigated. Four were men and 6 were women; their average age was 45, ranging from 29 to 69. The clinical data are summarized in Table I which shows their pre-operative diagnosis, the operative procedure, the duration of follow-up, their anxiety and tension scores, and the result of the operation. The latter was classed as *successful* when the patient's symptoms were relieved and their occupational and domestic adjustment was as good as it had been before their current illness; as *improved* when their symptoms were relieved and they were able to leave hospital, but unable to fulfil adequately their domestic or occupational roles; and as *unimproved* when their symptoms persisted and they were unable to leave hospital.

Results

A. *Autistic Gestures in Patients and Healthy Controls*

The spontaneous movements were counted in 15 healthy males and in 10 patients (4 male and 6 female) selected for leucotomy, while they sat alone for two periods of 10 minutes. The movements were of the self-directed kind already referred to as autistic gestures. The procedure was identical for both groups.

TABLE I

Patient	Sex	Age	Diagnosis	Operation	F.U. (mos.)	Result	Anxiety and Tension Scores: Pre-op.	Anxiety and Tension Scores: Post-op.
H.E.L.	f	29	Anorexia Nervosa with Depression	Pre-frontal leucotomy (Poppen)	12	Improved	7	4
W.A.S.	m	33	Obsessional: Abnormal personality	Topectomy 9 and 10	12	Successful	2	2
R.F.S.	f	33	Obsessional-compulsive syndrome with depression	Pre-frontal leucotomy (Poppen)	12	Improved	8	2
A.R.K.	f	37	Paranoid Schizophrenia	Topectomy 9 and 10	3	Unimproved	3	5
F.N.	m	56	Involutional depression with obsessional features	Topectomy 9 and 10	12	Successful	6	0
L.A.A.	f	44	Chronic Depression: Psychopathic Personality	Pre-frontal leucotomy (Poppen)	12	Improved	8	0
E.E.T.	f	50	Agitated Depression Paranoid	Undercutting 9 and 10	3	Improved	5	0
H.J.H.	m	42	Tinnitus: Reactive Depression	Topectomy 9 and 10	6	Successful	8	1
A.H.	m	69	Involutional Depression	Pre-frontal leucotomy (Poppen)	6	Unimproved	4	3
A.E.G.	f	62	Involutional Depression	Pre-frontal leucotomy (Poppen)	3	Successful	5	2

The mean score of the healthy controls was 8·62 counts per minute (σ8·51), and that of the patients was 19·56 counts per minute (σ14·30). The difference between these means is significant at the 2·5 per cent. level (t=2·31). This finding was in the predicted direction, namely, that emotionally disturbed subjects would have more autistic movements.

B. *Changes in Spontaneous Movements after Leucotomy*

The mean number of autistic gestures scored per minute by 10 patients while sitting alone and unoccupied was 19·56 before the operation and 7·31 three months to a year after it. This decrease is significant at the 2·5 per cent. level (see Table IIA). If the 2 patients who were not improved by the operation are omitted the decrease then becomes significant at the 0·5 per cent. level (see Table IIA).

TABLE IIA

Mean change in autistic movements following leucotomy

		Mean No. Movements/Min.		Standard Deviation			
No. of Patients		Before Op.	After Op.	Before Op.	After Op.	t	P
Total Group ..	10	19·56	7·31	14·30	2·70	2·39	·025
Successful or improved	8	22·45	7·34	14·02	6·07	2·59	·005

TABLE IIB

Mean change in communicative movements following leucotomy

		Mean No. Movements/Min.		Standard Deviation			
No. of Patients		Before Op.	After Op.	Before Op.	After Op.	t	P
Total Group ..	10	21·00	10·35	13·08	5·33	2·27	·025
Successful or improved	8	24·25	10·96	10·40	5·60	2·93	·005

When each patient's scores are considered separately, it is found: in 7 out of the 10 there is a significant decrease in movements following the operation; in 2 patients the differences are not significant; and in one (A.R.K.) there is a significant increase. The latter patient sat quite motionless before the operation, even

her blinking was only occasional, whereas after it a few small movements were recorded. She was not improved by the operation. The other patient who was not improved showed a significant decrease in movements (see Table III).

The findings during the interview period, which gave a measure of communicative movement, were similar. The mean score for the 10 patients after operation was also significantly lower than before (at the 2·5 per cent. level); the significance increased to the 0·5 per cent. level when the 2 unsuccessful patients were omitted (see Table IIB). Considered individually, 9 of the patients' movements decreased, 8 of them significantly; but the same patient as before (A.R.K.) was found to have a significant increase in movements. Again 1 of the unimproved patients showed a significant decrease and 1 a significant increase (see Table III).

Few as the patients are, it appears that following operations of this kind a decrease in spontaneous movement is to be expected; and as one of the two patients whose mental condition was unimproved also showed a significant decrease it is unlikely that a clinically successful result is essential to bring about the change. The relation between change in mental state and movements is investigated further in the following section.

C. *Relations between Mental State and Changes in Spontaneous Movements after Leucotomy*

1. Mental state: the 5 patients in whom depression was the predominant feature differed from the 5 patients with obsessional and paranoid features. Following the operation the mean decrease in movements made by the depressives was 21·9 counts/min., but the paranoids and obsessionals decreased by only 2·6 counts/min. This difference is significant at the 0·1 per cent. level (the sample variances did not differ).

Both the patients whose spontaneous movements increased were markedly paranoid. They both tended to sit motionless but alert before and after the operation, their posture and movements becoming a little less guarded following it. The change in movements recorded seemed to parallel their slightly diminished suspiciousness after leucotomy. The pre-operative movement scores of both were low and provided little opportunity for any further decrease. The most restless patients pre-operatively were those who showed the greatest decrease following the operation; the product-moment correlation between the pre-operative scores of spontaneous movements and decrease in scores was −0·93.

The relationship between mental state and autistic gestures was further investigated by finding the product-moment correlation between the patients' pre-operative scores of spontaneous movements made while alone and their clinical ratings for anxiety and tension. This was found to be 0·704, which is significant. Similarly, there was a significant correlation between the decrease in anxiety and tension scores and the decrease in movement scores following the operation.

Those patients, therefore, who showed the most affective disturbance, such as depression and tension, were those who had most spontaneous movements and whose spontaneous movements decreased the most following leucotomy.

2. Age and sex: there was no consistent relation between age or sex and change in movements following leucotomy—the tendency reported by Kinder *et al.* (1952) for movements to decrease in the elderly and increase in the younger patients was not observed.

TABLE III

Patient	Sex	Age	Mean Moves per Minute (Alone)						Mean Moves per Minute (Interview)					
			Pre-op.	Post-op.	Difference	SE_D	t	P	Pre-op.	Post-op.	Difference	SE_D	t	P
H.E.L.	F	29	50·4	20·2	—30·2	4·80	6·28	>·001	38·7	24·0	- 14·7	2·87	5·15	>·001
W.A.S.	M	33	8·8	3·0	—5·8	1·35	4·30	>·001	15·6	6·9	—8·7	1·63	5·35	>·001
R.F.S.	F	33	22·9	11·3	—11·6	4·63	2·51	>·02	23·8	14·5	—9·3	2·93	3·15	>·01
A.R.K.	F	37	0·8	5·3	+4·5	1·35	3·38	>·01	0·4	4·9	+4·5	0·68	6·67	>·001
F.N.	M	56	11·9	11·4	—0·5	3·29	0·15	n.s.	22·2	9·0	—13·2	4·49	2·94	>·01
L.A.A.	F	44	26·6	2·5	—24·1	3·27	7·37	>·001	21·6	11·5	—10·1	3·25	3·11	>·01
E.E.T.	F	50	2·3	2·7	+0·4	1·43	0·28	n.s.	10·6	5·5	—5·1	3·36	1·50	n.s.
H.J.H.	M	42	32·5	1·7	—30·8	4·83	6·39	>·001	48·0	9·0	—39·0	4·60	8·48	>·001
A.H.	M	69	15·2	9·1	—6·1	2·47	2·46	>·05	17·4	10·9	—6·5	4·57	1·42	>·001
A.E.G.	F	62	24·2	5·9	—18·3	3·23	5·68	>·001	11·7	7·2	—4·5	2·19	2·06	>·01

D. *The Effects of Differing Operations on Spontaneous Movements*

It was found (see Table III) that autistic gestures decreased after leucotomy in 7 out of the 8 successful cases, and that movements during interview decreased in all the 8 successful cases. Of the 2 patients whose operation did not lead to improvement, 1 showed a significant decrease in autistic gesture and in communicative gesture. Evidently the pre-frontal leucotomy can be followed by reduced movements without any concomitant reduction in anxiety and tension. The problem then arises whether certain pre-frontal areas may not exercise some direct physiological control of spontaneous movements.

As the surgical procedure varied from patient to patient an attempt was made to differentiate the effects of the leucotomy cuts. The operations were of three kinds; open pre-frontal leucotomy, topectomy of areas 9 and 10, and undercutting of areas 9 and 10. The changes in movements following the two operations which isolated areas 9 and 10 were compared with those following the more extensive cut of the open pre-frontal operation. In all the 5 patients who had the latter a significant decrease in movements was found; but only 2 out of the 5 patients who had a topectomy or undercutting of areas 9 and 10 showed significant decreases, and 1 showed an increase. However, no conclusions may be drawn, because the numbers are too few and the more anxious patients had mostly had the open leucotomy and the less anxious the localized operation. These two operations were not well suited to the purpose of comparing the effects of ablating different pre-frontal areas on spontaneous movements: the work quoted already suggests that differences might be more profitably sought between medial cuts isolating the orbital areas and cuts isolating areas 9 and 10.

E. *The Characteristics of Gestures Compared before and after Operation*

The autistic and communicative gesture scores attained during 20 sessions were correlated. The high value obtained ($r=0\cdot9 \pm 0\cdot026$) suggested that the factor which determines a high score in one category of expressive movements also affects the other.

The records were examined next to find whether the ratio of autistic to communicative movements differed before and after the operation. If, as Petrie and Crown found, patients become more extroverted following leucotomy, they might be expected to decrease communicative or social movements relatively less than autistic ones. In 8 out of 10 patients the communicative movements were found to decrease in this way. The probability that this result could be due to chance was tested by χ^2. The value obtained, $3\cdot60$ ($P>0\cdot1$), is below the 5 per cent. level of significance ($3\cdot84$). The finding, however, is in the predicted direction and would justify an enquiry made with a larger number of patients.

The autistic gestures of each patient were studied from the films taken while he sat alone before and after operation. It was very evident that each patient had his individual mannerisms which, in a similar situation, regularly recurred. Leucotomy did not prevent the reappearance of his characteristic autistic gestures, but changed their frequency, the emphasis with which the movements were made, and diminished many of the repetitive, superfluous movements. The nail biter, for instance, continues to bite his nails following the operation, but in a leisurely manner instead of urgently. This change in emphasis may be a consequence of the decreased muscle tension which was also found to follow leucotomy.

Summary and Conclusions

A method of measuring spontaneous movements by integrating the action potentials which accompany contractions of the extensors of the fingers and wrists is described. The method was found to give a valid measure of spontaneous movements, and the test-retest reliability of the movement scores was satisfactory.

Spontaneous movements were measured in patients selected for leucotomy (*a*) while they sat alone and unoccupied, and (*b*) during interview; in the former situation autistic movements only were observed, in the latter communicative gestures predominated.

Before leucotomy the patients were found to make significantly more autistic movements than did the healthy controls. The patients made significantly fewer autistic and communicative movements after leucotomy than they did before it.

Three features in the pre-operative mental state were significantly associated with the decrease in movements following leucotomy. They were anxiety and tension, depression, and restlessness.

One patient, however, who was not improved by the operation, was also found to make significantly fewer movements following the leucotomy: section of the pre-frontal white fibres in this instance decreased movements independently of change in the mental state.

The more extensive operation was consistently followed by a decrease in movements, but the operation localized to areas 9 and 10 was not. This finding could not, however, be ascribed to differences in the extent of the leucotomy cuts as the mental states of the two groups were not comparable.

Communicative movements (social) decreased relatively less than the autistic (self-directed) in 8 out of 10 patients suggesting a tendency to increased extroversion following the operation. The autistic mannerisms peculiar to each patient were unaltered by the operation, but occurred less emphatically when there was diminished muscular tension after the leucotomy.

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A METHOD OF MEASURING SPONTANEOUS MOVEMENTS BY TIME-SAMPLING MOTION PICTURES

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In the course of planning a research into spontaneous movements (expressive movements and disorders of involuntary movement, such as tics), it was essential to devise some means whereby these forms of motor behaviour might be objectively measured. The purpose of this paper is to describe one of our methods of doing this by the use of motion pictures, and to demonstrate experimentally the reliability and validity of a method which, it is believed, may prove to have a wider application.

Before outlining the method the two principal categories of movement it was designed to assess will be briefly described.

A. *Expressive Movements* which may be divided into:

1. Those subserving communication with others which, as a rule, accompany speech, especially its emotional references.

2. Autistic gestures. These, Krout (1935) has suggested, are concerned with "communication with the self", because some movements, which may be treated as meaningless by the observer, were found to have specific, autistic significance to the performer. Examples of the kind of behaviour subsumed under this term are many so-called "nervous habits" and "mannerisms" of an individual; nail biting, picking, adjusting tie, etc. Being alone, preoccupied, or in a state of stress appears to favour their occurrence.

B. *Disorders of Movement* of uncertain aetiology, but in which there is some evidence to suggest that the mechanisms disturbed are related to those serving expressive movements: tics, torticollis and hyperkinesis.

The technique to be described was developed from a method devised by Olson for measuring nervous habits in normal children (Olson, 1929). It yielded scores whose reliability could be determined. The children were observed directly; and the unit of measurement was defined as one or more specified nervous movement per stated unit of time.

This time-sampling method enabled Olson to measure nervous manifestations and relate them to age, sex, family history and so on. Others (Koch, 1935; Seham and Boardman, 1934; Young, 1947) have extended his observations, while Jones (1941) has used the method to study nervous movements in adult psychotic patients.

When frequently repeated movements, such as gestures, are to be measured, recording them cinematographically and subsequently scoring the film offers a number of advantages.

1. A film provides an unlimited opportunity for accurate measurement because it can be projected as often as is necessary to obtain a consistent and therefore reliable score.

2. Consequently a relatively shorter period of observation is required than with the less reliable method of direct observation; this is often an important practical advantage, particularly when studying disturbed patients.

3. The method is less fatiguing to the observer. Time-sampling by direct observation using periods of only a few seconds is tiring and difficult, and therefore inaccurate.

4. When only one trained observer is available and the experimental design, or mental state of the patient, requires him to be with the subject, the desired record is still obtainable.

5. Finally, when movements are repeated so rapidly that time-samples of 2 seconds or less are required to study their variations, counting by direct observation becomes too difficult (e.g. certain tics, and the conversational gestures of some); but cine-photography with the camera speed increased (slow-motion) makes their measurement possible.

Apparatus and Procedure

As self-consciousness is likely to modify many forms of spontaneous and gestural movement, the camera (a Paillard Bolex H16) was arranged so as to be neither audible nor visible to the subject. The subject sat close to a baize covered table. This arrangement, without imposing any sense of restriction, tended to favour gestural movements in the arms and ensured their occurrence against an even and satisfactory background.

Above and in front of the subject there was a 200-watt lamp, a 500-watt five feet to his right-front, and a 200-watt four feet to his left. These lamps were in the standard hospital fittings and rarely provoked any comment. This lighting proved to be adequate when filming at 16 frames per second, using fast film (Kodak Super XX), and an aperture of f.2·8.

The distance of the camera from the subject was adjusted so that with a 1-inch lens the field included the subject's half-figure and the whole of the table top; a 3-inch lens was used for close-ups of facial movements.

Finally, a folding screen behind the subject provided a suitable background and also served to support a small 12-volt bulb which was in circuit with an adjustable timing unit. Depending on the expected frequency of the movements to be scored, the light was set to switch on for periods of $2\frac{1}{2}$ or 5 seconds, switch off for an interval of the same duration, then on again, and so on.

Fifteen seconds after switching on the timing light, the camera was started and ran for 45 seconds, being stopped at the minute. During the following minute the camera was rewound and at 15 seconds past the third minute the process was repeated. In this way five 45-second samples (each made up of either nine 5-second units or eighteen $2\frac{1}{2}$-second units) of the subject's movements during alternate minutes were obtained from 100 feet of film.

Scoring

The processed film was projected and the movements scored as follows:

An observer watched the film while his assistant recorded the counts (with a little practice the observer can perform both operations). The observer started counting when the timing light first flashed on. If during the ensuing 5 seconds (or $2\frac{1}{2}$ seconds as the case may be) when the light was on, the subject

was seen to make the movement to be studied one or more times, the observer called out "yes", and this was scored as 1 by the assistant; a movement, therefore, was scored once only per unit of time. Should the movement not occur the observer called "no". At the end of 5 (or $2\frac{1}{2}$) seconds the light goes off and stays off the same period of time; this interval was also scored. The maximum score for any 45 seconds, therefore, is 9 (or 18) and so for 100 feet of film it is 45 (or 90). On the basis of careful reliability studies on the time-sampling method (Olson, 1929; Jones, 1941), it was estimated that 45 observations would afford a satisfactory sample of a subject's movements.

In this way, with a little practice, an accurate score of the movements can be obtained, as can readily be shown by asking a second observer to repeat the procedure and then checking his score with that of the first. Should repeated differences in the total count occur, as may be the case where the movement studied is of a complex character, the instances in which the two observers differ are easily located on the score sheet. The equivocal movement may then be re-examined by the criteria on which it is agreed to define it and a decision whether to include it in the total agreed upon. It is the opportunity provided for repeated observation that gives the method its accuracy and value.

In our earlier observations we did not have a light flashing behind the subject. The films were then scored by placing the light alongside the screen on which the film was projected. This technique is a useful one if, when examining any film, it is considered that useful data may be obtained by quantifying the activity being observed.

The method having been described, it is now necessary to enquire whether in application it is both reliable and valid.

The first three experiments to be described are concerned with the reliability of the scores of various kinds of spontaneous movements.

Experiment 1

The aim was to estimate the reliability of the subjects' autistic movement scores obtained from time-sampling 100 feet of film.

Procedure. Twenty films, each 100 feet, were taken of the autistic movements of a group of healthy young soldiers while sitting alone. The films were scored in the manner described above. The scores obtained during each odd 45-second period were then correlated with those during the even ones.

Results. The reliability coefficient was 0·86; when this figure is corrected by the formula $\frac{2r}{1+r}$ the coefficient is increased to 0·93.

Experiment 2

The purpose was to see whether the scores obtained from five 45-second periods of filming of the autistic movements of the forearm and hands constituted a reliable sample of these movements occurring during a considerably longer period, 20 minutes.

Procedure. The movements scored from 25 films (100 feet) of healthy male subjects sitting alone were correlated with their movements scores obtained from 20 minutes of continuous measurement by means of an electromyograph with an integrating circuit.

The electromyograph (E.M.G.) is a powerful two-channel amplifier into which are fed the action potentials picked up by electrodes placed on the skin overlaying muscle. The amplitude and frequency of the potentials vary proportionately with the number of active motor units and their rate of discharging.

The amplified potentials may be recorded on an oscilloscope or by a pen recorder. In this apparatus they are also accumulated on a condenser which, when it is sufficiently charged, closes a relay and so operates a counter. In this way the electrical potentials accompanying activity in a muscle, or group of muscles, may be counted. By selecting a suitable setting of the gain on the amplifier, only the larger potentials which occur during movement will operate the integrating circuit and counters. The method is described in detail elsewhere (Sainsbury, 1954).

The subjects sat at the card table with the electrodes lightly strapped to the skin over the crest of the extensor muscles of the wrists and fingers. Each subject was left alone for 20 minutes. Forty-five-second exposures were made with the cine-camera during 5 alternate minutes. Thus the amount of autistic movement scores during $3\frac{3}{4}$ minutes was obtained from the films, whereas the E.M.G. measured the movements during 20 minutes. The mean movement score per minute was calculated from both sets of data and these were correlated.

Results. The product-moment correlation was 0·83 (see Table I). This

TABLE I

To show the autistic movements score per minute obtained from approximately 4 minutes of cine-film and 20 minutes of electromyographic recording

Film No.	Time-sample score per min.	Electromyograph score per min.
1	3·4	2·8
2	7·0	9·8
3	0·2	0·3
4	3·2	7·0
5	0·4	2·0
6	4·7	3·6
7	4·0	5·1
8	8·0	19·4
9	6·3	9·3
10	4·2	10·9
11	8·2	18·3
12	10·2	20·9
13	1·5	8·7
14	6·0	5·4
15	8·7	16·9
16	5·0	11·5
17	1·5	5·6
18	7·8	11·9
19	9·2	22·6
20	6·7	23·4
21	4·8	9·6
22	5·1	11·1
23	6·3	13·2
24	10·8	31·2
25	7·2	9·7

Correlation $r = 0{\cdot}830 \pm 0{\cdot}04$ (see footnote to Table IV).

result suggests that a 100 feet film which samples less than 4 minutes of the subjects' autistic movements was a reliable index of the amount of the same behaviour which occurred during 20 minutes.

Experiment 3

A further attempt was made to estimate whether a short film afforded a reliable sample of spontaneous movements (in this instance tics), by comparing the scores obtained from films with those obtained by direct observation of the tiqueurs during 12-30 minutes.

Procedure. The observations were made on 3 patients, 2 with facial tics and the other with multiple tics. In the first, the tics were counted while the patient sat alone, and also while he was reading. The tics of the other 2 patients were counted while they sat alone.

Forty-five-second exposures were made during alternate minutes until 100 feet film had been used. At the same time, but continuing for a longer period (see Table II), the tics were scored by direct observation of the patient through a one-way screen. The unit of measurement was the same as that used with the films, namely, one or more tics per 5-second period.

Results. The tic rates obtained by these two methods are compared on Table II, which also gives the number of 5-second units of observation made on each tiqueur by both methods. The rates obtained by the different methods are

TABLE II

Compares the number of Tics per minute obtained from patients by direct observation time-sampling and by time-sampling films during a shorter period

Patient	Circumstances	No. of 5-sec. units in direct observation period	No. of 5-sec. units in filming period	Score/min. by direct observation	Score/min. by cine-film
A.J. ..	Reading alone	216	44	1·0	1·1
	Alone	180	44	2·5	3·0
L.S. ..	Alone	144	50	9·5	9·1
P.S. ..	Alone	396	88	2·7	2·8

not significantly different. In the first case there is a dimunition of the tics when the patient's attention is occupied by reading, so a common clinical impression was objectively and quantitatively confirmed.

Experiment 4

This was to investigate the validity of the method by comparing the scores for autistic gesture obtained from films with those derived from two other methods. In this experiment, in contrast to the previous two, the movements were scored from the films and by the alternative methods recording concurrently with the camera.

Procedure. In the first method 12 films (100 feet reels) of seven subjects were taken as they sat alone at the table.

Five 45-second exposures of the subject's behaviour were obtained and scored in the usual manner by counting the number of 5-second units in which the movements were discerned. At the same instant as the cine-camera's 45-second runs were started, a time-sample by direct observation through a one-way screen was begun and continued till the camera stopped. The time-sample scores obtained from the films were then correlated with the simultaneous time-sample scores obtained by direct observation.

Results. The findings from 12 films and direct observation scores showed a satisfactory correlation (r=0·998, see Table III).

TABLE III

Compares the time-sampling scores of autistic movements obtained from 3¾ minutes of cine-film with those obtained by direct observation during identical periods

Film No.	Film time-sample Score per min.	Observed time-sample Score per min.
1	0·0	0·0
2	0·6	0·8
3	3·4	4·9
4	7·0	7·9
5	0·2	0·3
6	3·2	3·3
7	0·4	0·0
8	8·5	10·2
9	10·5	11·7
10	4·7	5·1
11	4·0	6·1
12	8·0	8·9

Correlation r=0·998 ±0·001.

In the second method a similar procedure was adopted, but on this occasion the film scores were correlated with those obtained on the E.M.G. counters during the same 45 seconds. Twenty films and electromyographic recordings of 10 subjects were obtained. The product-moment correlation was 0·87 (see Table IV).

TABLE IV

Compares the time-sampling scores of autistic movements obtained from 3¾ minutes of cine-film with those obtained by electromyograph measurement during identical periods

Film No.	Film time-sample score per min.	Electromyograph counts per min.
1	21	24
2	14	34
3	25	69
4	20	54
5	5	17
6	20	45
7	31	62
8	15	34
9	16	33
10	17	45
11	5	19
12	26	34
13	29	77
14	18	51
15	15	15
16	22	44
17	2	1
18	25	55
19	11	20
20	0	4

Correlation r=0·87 ±0·04.

This correlation is less than that found when film scores are correlated with direct observation scores. The lowering of the correlation may be ascribed to the fact that the counts scored by the electromyograph will depend not simply on the presence of a movement (the factor determining the film score) but also to some extent on the duration and the intensity of the muscular effort.

Summary

1. A method is described of measuring spontaneous movements by time-sampling films.

2. This method is to be preferred to direct observation if frequently occurring movements are being studied because it is more accurate, less fatiguing, requires shorter periods of observation, and leaves the experimenter free. By using slow-motion, time-samples in units of 1 second are possible.

3. The split-half reliability of the movement scores obtained from the films was 0·93.

4. In two experiments it was found that an economical amount of film afforded a reliable sample of the subjects' movements. In the first, the autistic movements scores obtained from time-sampling 100 ft. of film correlated highly with the scores obtained from counting them with an E.M.G. during 20 minutes ($r=0·83$).

In the second, tics were scored from short films and compared with the scores found during 12-30 minutes of direct observation. The results corresponded closely.

5. The validity of the method was tested: (*a*) by correlating the time-sampled scores of autistic movements obtained from films and from observation during identical periods ($r=0·998$); (*b*) by similarly correlating the film scores and E.M.G. scores of the movements obtained concurrently ($r=0·87$).

6. Although the numbers investigated were small the results suggest that the method is a reliable and valid one.

Acknowledgments

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DISORIENTATION FOR AGE

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THIS note is intended to supplement Professor Zangwill's communication (1953) under this title in the centenary number of this journal, in which "disorientation for age" as described by Weinstein and Kahn (1950 and 1951) is illustrated as persistent and stable in two cases of alcoholic Korsakov psychosis.

Both these patients are described as orientated for year of birth and current year, yet they underestimate age by 16 years and 10 years respectively. This tendency to maintain disorientation in the face of contradictory evidence is viewed as an example of the entertainment of incompatible propositions in amnesic states, first described by Pick in 1915. Even though able to do the arithmetical reasoning involved, both patients did not accept the result as their "actual" ages. In discussing this phenomenon, Zangwill expresses the view that in both cases the concomitant retrograde amnesia and certain motivational factors were responsible for the disorientation and its tenacity.

Evidence from another, but related, field is presented here to show that similar disorientation for age can occur temporarily, and also that orientation for age can be present, even without the data of birth year and calendar year necessary for the arithmetical calculation.

The evidence is taken from part of a pilot study of the recovery of consciousness after electro-convulsive therapy, somewhat on the lines of the investigation reported by Lunn and Trolle (1949). Examination for autopsychic and allopsychic orientation, perception, memory, etc., was carried out during the recovery period after treatment by standard and diphasic steep-wave electroplexy (Strauss and MacPhail, 1946).

The relevance of observation upon recovery from E.C.T. to Korsakov psychosis is based on the contemporary electro-encephalographic and clinical observations upon the similarity of biological and psychological changes in Korsakov psychosis, post-traumatic states and recovery of consciousness from E.C.T. Such observations are marshalled by Roth (1952) to suggest that the primary effects of E.C.T. are on the diencephalon. Some authors have suggested that a full-blown Korsakov syndrome can be produced by E.C.T. However, in view of the fact that the classical Korsakov syndrome extends beyond such psychological effects, it is perhaps best to speak of a Korsakov-like state, to refer to this condition of patchy amnesia and disorientations. This Korsakov-like state after E.C.T. can be observed transitorily during the recovery from each treatment and sometimes, especially in arteriopathic patients, more prolongedly after a full course of treatment.

Whereas in the investigations by Lunn and Trolle, a series of questions was asked at intervals of 10, 30, 60, and 120 minutes after shock, in the present investigation, testing was carried out continuously from the time that the patient

showed some response to a stimulus, such as a handclap. The whole examination took on the average 45 minutes. Orientation for name and other matters of personal identity were usually first to be established and examination was continued until the prepared set of questions (25 in all) had been answered. Only part of the results are reported here—namely those concerned with orientation for name, age, year of birth, and for the current year. Each question was asked at intervals of 5 seconds and if it was not answered after 15 seconds (3 repetitions) the next question was asked.

The eleven patients reported (7 female and 4 male) were being treated as out-patients. All were of average or above average intelligence, and were diagnosed as suffering from depressive illness. All were subsequently regarded as improved after completing a course of treatment.

The table shows the time to the nearest minute at which each question was answered correctly. In the full-scale investigation, timing was to the nearest 5 seconds. As in clinical examination, a correct answer to the question was taken as evidence of orientation. The view was taken throughout that orientation, once established, would remain intact. This was in general confirmed. The observations quoted were all carried out during recovery from the first treatment of a course. Further observations have shown the tendency for orientation for age to return earlier with each successive treatment. This finding may support the rehearsal effects discussed below.

Orientation for name is given here as a baseline of earliest recovery. This was found to be the case, although in fact ability to count fingers sometimes preceded name. As might be expected, some married women gave their maiden names before married names. This was so in Cases 1, 2, and 4 where maiden names were given at 8, 7 and 6 minutes respectively after shock. These patients had been married for a period of over 10 years.

During questioning, no attempt was made to give clues to the patient. The procedure was adopted of keeping the questions in a standard order of groups of five, and of dropping each question as it was answered satisfactorily. It was noted, however, that the juxtaposition of related questions and answers often did not produce insight, probably reflecting again Pick's state of entertainment of incompatible propositions in amnesias. The following illustrates a commonly found sequence:

Q. What is your name?
A. Mary Smith.
Q. Are you married?
A. Yes.
Q. What is your husband's name?
A. James.
Q. James what?
A. James Brown.
Q. What is your name?
A. Mary Smith.

From the table it is seen that in Cases 1, 2, 6, 7, 8, 10 and 11, the order of return was year of birth, age, current year. In these cases the correct answer to the question "What age are you?" succeeded the correct answer to "In what year were you born?", but preceded the correct answer to "What year is it now?" Cases 4 and 9 were orientated for age before they were orientated for current year and year of birth. In case 3, age and current year are given correctly by 23 minutes after shock. In actual fact, to the nearest 5 seconds, the correct

TABLE

			Time (minutes) after shock of orientation for			
			Name	Age	Year of Birth	Current Year
Females	1	aged 51	12	28	24	35
	2	„ 46	15	18	17	19
	3	„ 34	10	23	22	23
	4	„ 42	14	14	18	17
	5	„ 48	7	29	20	26
	6	„ 50	8	22	15	28
	7	„ 46	9	26	24	28
Males	8	„ 38	6	26	7	32
	9	„ 28	9	11	15	20
	10	„ 35	10	16	14	21
	11	„ 31	12	18	17	24

answer to age was given at 22 minutes 40 seconds and to year at 22 minutes 50 seconds, but where such a short time has elapsed between correct answers, the order of questions must play a large part in determining the priority of recovery. Case 5 is the only case in this series in which the facts of year of birth and current year were known before age was known.

Such measurements are too crude and the number of cases too small to support any conclusion beyond the demonstration that in these cases at least, orientation for age could occur without the knowledge of year of birth and current year.

It may well be that knowledge of age is not mainly dependent upon arithmetical inference, but stands as an isolated fact, changing through time and being maintained by rehearsal. Motivational factors, as Zangwill suggests, must also be considered. Results in a larger number of cases show that men on the whole tend to be able to give their correct ages sooner after shock than women. Further, it seems that women are more likely to show disorientation by saying they are 10 years younger than they actually are, whereas men express their disorientation by not knowing or not remembering their ages. Even on the basis of rehearsal effects, this difference may arise from the cultural fact that men, on the whole, are more likely to rehearse in their occupations (e.g. wage-scales linked to age, etc.). However, if this rehearsal effect were entirely true, then an age-difference in orientation for age might be expected, because the younger person with more likelihood of changing his employment or entering into contracts, such as insurance, marriage and so on, will have had more opportunity to rehearse age. Again the wider investigation has not yet shown a clear age-difference.

As in so many clinical discussions of negative symptoms the psychology of the normal positive features is lacking. The absence of any specific psychology of knowing one's age is a handicap in the discussion of the pathology of not knowing one's age. In general terms it could be speculated that factors of personal identity, such as age, would have stronger psychological force than the mere result of an arithmetical calculation. Zangwill points out that the denial of age in amnesic individuals has a protective function of allowing the individual to maintain as stable and consistent an orientation to himself and his situation as his cerebral condition permits. In terms of ego-psychology, the individual is trying to maintain the greatest possible intactness or integrity of his ego.

However, if we assume an organized body of memories which can be ordered in time as one requirement of the integrated ego, then it is difficult to

reconcile the fact that during recovery from E.C.T. it is quite common, for example, for a married woman to give her correct address, say that she is married, yet give her maiden name and her age as younger than at the date of marriage. If the desire to maintain intactness of the ego were wholly operative, then one would expect that all her answers would be relevant to her situation before or after marriage, depending upon the state and degree of her recovery. This point, however, may be merely the marginal point of which the psychological changes occurring in the temporarily produced and rapidly resolving organic state of E.C.T. are no longer comparable to the relatively more permanent and severe organic pathology of, say, the Korsakov psychosis.

Summary

The times at which orientation for name, age, year of birth and current year was re-established after E.C.T. are listed for 11 depressive patients treated by standard steep-wave electroplexy. It is suggested that orientation for age is not entirely dependent upon the presence of the ability to reason arithmetically, as in most of these patients orientation for age returned before orientation for both facts needed for such arithmetical inference, namely year of birth and current year.

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RORSCHACH RESPONSES OF A GROUP OF ADULT ASTHMATICS

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Introduction

Personality characteristics of patients suffering from bronchial asthma have attracted considerable attention. Most clinical observations suggest that asthmatics present a characteristic difficulty in emotional expression. Reporting on the behaviour of 23 children with either asthma or eczema, Rogerson, Duguid and Hardcastle (5) state that these children were more shy than others in play therapy. Harris *et al.* (3) compared asthmatic children to children with allergic rhinitis. They suggested that half of the asthmatic group showed more difficulties than the rhinitic group in crying and confiding to the mother. These observations were made on children. On the adult side we have the inferences of French and Alexander (2) (based on psychoanalytical situations) that the asthmatic attack is the equivalent of a suppressed cry. However, as Leigh (4) has pointed out in his recent review of the psychiatric aspects of asthma, little valid evidence has in fact been presented that this feature of personality or any other is characteristic of asthmatics. This paper is a report on findings which may be related to this lack of evidence.

Material and Methods

Thirty adults suffering from asthmatic attacks were given the Rorschach test. They formed a highly selected group, in that all had been referred to a psychiatrist particularly concerned with the study of this disorder. However, the clinical findings differed in no way from what has been found in larger groups of asthmatics—there were roughly the same proportions of allergic or infective factors, hereditary incidence and sex distribution. Their ages ranged from 15 to 53 years, with a mean age of 31 years 10 months. They had suffered from asthmatic attacks for periods ranging from three months to forty years (approximate mean—12 years). Twenty were women, and ten men; their I.Q.s as measured on Raven's Progressive Matrices were between 84 and 129 (approximate mean I.Q. 108·7) (5 patients had not been tested for intelligence level, an assessment was made from a scrutiny of the history).

The Rorschach was given in the standard fashion, after the subjects had seen the psychiatrist for a preliminary interview. In all but two cases the test was given before treatment had begun. Fourteen were tested by the writer, and 16 by a variety of psychologists. All patients were in an asthma-free period at the time of testing.

Results

The most striking feature of these records is their overall restriction and in this paper attention will be confined to the number of responses as an objective

measure of that restriction.* The average is 24 (standard deviation=12·24). Moreover this simple objective measure appears to have a certain degree of generality with regard to asthmatics. Schatia (6) concluded from her interpretation of the Rorschach records of 40 asthmatics that most of them were neurotics. In fact, what her tables showed as the most consistent feature of those records was the low number of responses (less than 30, in 38 out of 40 records). Vles en Groen (7) showed there was a significant difference in the number of responses between an asthmatic group and a healthy control group both tested on the Behn Rorschach.

Comparison with Other Populations

The average number of responses for our group of asthmatics is 24 and falls well below that expected on the Rorschach from an averagely intelligent population. Beck and his co-workers (1) obtained on a population of 157 Americans with similar age range a mean number of responses of 32 (standard deviation=17). The difference between the two populations was assessed by a t-test

$$t=\frac{\bar{x}_1-\bar{x}_2}{\sqrt{\frac{\sigma_1^2}{n_1}+\frac{\sigma_2^2}{n^2}}}=3\cdot2$$

and is significant at the 0·01 level. However, the comparison with an American group was unsatisfactory, as cultural characteristics could have partly accounted for that difference. So the asthmatic group was compared with a carefully matched control group of 30 neurotic patients from a similar background. Each asthmatic patient was paired with a neurotic patient of the same sex, age and intelligence (Table I).

Table I

	Mean Age	Approx. Mean I.Q.
Asthmatics	31 years 10 months	108·7
Neurotics	31 years 5 months	109·5

Most of the age differences were between 1 and 5 years. Only in the upper age range was there one difference of 8 years and one of 12 years. Most of the I.Q. differences (which again had in some cases to be approximately evaluated) were between 0 and 5 points. The highest was of 8 points.

(1) *Difference between the Means*

The mean number of responses for the neurotic group was 32·1 (standard deviation=16). The distribution of differences in the number of Rorschach responses for each pair was plotted and found to be normal. The variance of differences was therefore used as a basis for the t-test, thus allowing for the use of the raw data instead of their logarithmic equivalents. The formula used was the one most appropriate for the comparison of paired correlates:

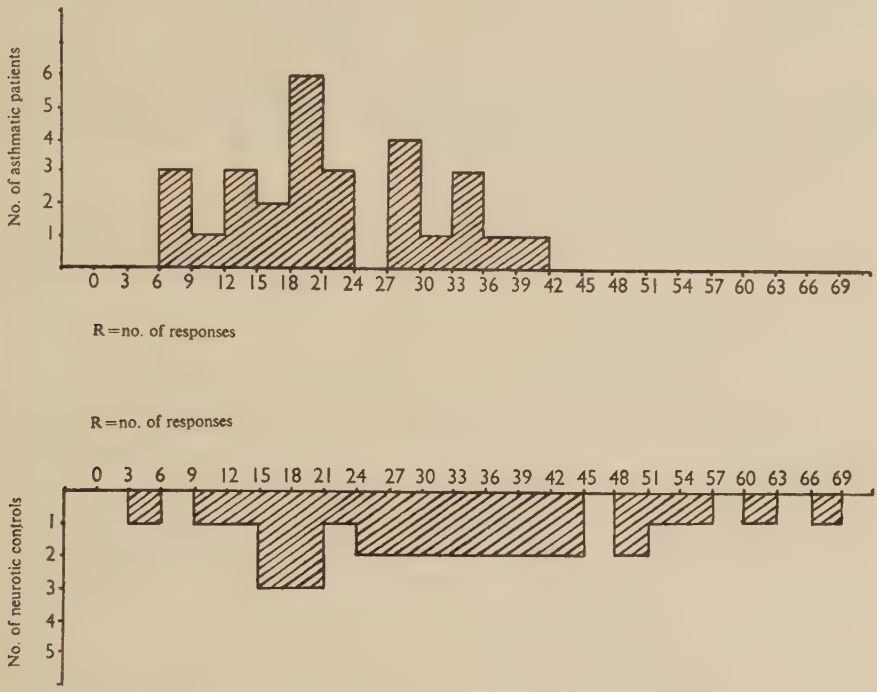
$$t=\frac{\bar{x}_1-\bar{x}_2}{\sqrt{\frac{\Sigma d^2}{n(n-1)}}}=2\cdot486$$

* Almost every scorable feature of any given Rorschach record is related to this one measure and it is difficult to evaluate differences in Rorschach determinants (whether these are calculated in absolute numbers or in percentages) unless the records present roughly the same number of responses.

The difference between the two groups in terms of the numbers of Rorschach responses was significant at the 0·02 level.

(2) *Distribution*

This is represented in the following graph (Fig. 1). Asthmatic subjects it may be observed are not consistently below their control neurotics in the



number of responses. However, only one of the asthmatics (3 per cent.) attained a score of 42 (half a standard deviation above the mean for the normal population), whereas 8 of the neurotics (25 per cent.) gave a higher number of responses. In other words, neurotic patients give very short as well as very long records, whereas asthmatic patients give very few long records.

(3) *Comparison between Men and Women*

When comparing the records given by men with those from women it can be seen that the differences noted in 1 and 2 almost entirely result from the very low number of responses given by the women patients suffering from asthma (Table II).

TABLE II

	Mean Responses
30 Asthmatics	24
30 Neurotics	32·1
20 F. Asthma	21·7
20 F. Neurotic	31·1
10 M. Asthma	28·5
10 M. Neurotic	30·2

In our two groups there is a higher proportion of men than women with an I.Q. above the mean (in this population the mean is 108 to 109). It was therefore advisable to compare only those asthmatics and controls with an I.Q. above the

mean. Table III shows that the difference becomes even more marked, and that intelligence plays no part in it.

TABLE III

	Mean number of Responses		Mean number of Responses
11 F. Asthma ..	23·1	8 M. Asthma ..	31·7
11 F. Neur.	35·1	8 M. Neur.	31·0

However, with such small groups results do not attain significance. In Vles en Groen's (7) group, of men and women, the findings are in the same direction although the differences are less striking because of the lower overall productivity of his group (Table IV).

TABLE IV

	Mean number of Responses
Control group	21
Asthma. Men	20
Asthma. Women	15

It seems to the writer that the neurotic group presented here is less varied in its number of responses than would usually be expected. Two reasons may have contributed to narrow the spread of the neurotic distribution:

(i) All these records were of patients for whom a psychological examination had been requested by the psychiatrist. Very hostile, retarded or almost untestable neurotics would have added to the number on the low end of the curve, but would justifiably be excluded as not comparable to our very co-operative group of asthmatics;

(ii) When matching the two groups the writer purposely rejected two neurotics who would have been adequate for criteria of age, sex and intelligence, but whose records were, respectively, of 135 and 190 responses; it was felt that they would spuriously inflate the mean.

A larger and less selected group of neurotics would probably have had a wider distribution in terms of number of responses—and because the Rorschach allows for a practically unlimited number of responses, the results would have probably been even more significant.

These findings are of interest as they are consistent with a clinical impression widely accepted among psychiatrists. The test situation can be taken as representing a comparatively standardized stressed situation which might be analogous to a life situation. Faced with it the asthmatic patient is generally restricted in his responses, and less capable of expression than normals or neurotics.

Two points must, however, at once be put forward. Firstly, no evidence is presented here to suggest that this restricted number of responses is specific to asthmatics and not, for instance, related to any chronic illness, or only apparent in those asthmatics who seek psychiatric help. The second objection is pertinent to the nature of the Rorschach. With a test of so many facets we do not know which factor in the test-situation or in the test-stimulus has affected the number of responses in that way. It would seem important to test the asthmatic reaction to simpler perceptual tasks or to other tasks involving choice or verbal communication.

Summary

1. A group of adult asthmatics showed, when compared to a normal population, a significantly lower average number of responses to the Rorschach.

2. The same group, when compared with a carefully matched group of neurotics, also showed a significantly lower number of responses.

3. Only 3 per cent. of the asthmatic group as against 25 per cent. of the neurotic controls reached above a score of R=42.

4. These results are of interest in view of the reported clinical assumption that asthmatics are inhibited in their mode of expression.

5. The asthmatic women were more restricted than the men in their responses to the Rorschach.

Further studies should include first a confirmation of these findings by bringing in more control groups for comparison; then an investigation of the causes which lead to a restriction of responses to the Rorschach.

Acknowledgments

I wish to record my gratitude to Dr. D. Leigh who provided the clinical facilities for this work to be undertaken, and whose enthusiastic encouragement and concrete help brought it to completion. I also wish to thank my colleagues, especially Mr. Shapiro and Dr. Ehrenberg for their helpful criticism.

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Reviews

Group Psychotherapy. By FLORENCE POWDERMAKER, M.D., and JEROME D. FRANK, M.D. Harvard University Press, 1953.

The dynamics of group interaction and the potential possibilities of treating patients collectively, instead of individually, are only just beginning to be explored. Group therapy, like individual therapy, will probably always remain more of an art than a science, for to apply to a therapeutic group the experimental limitations necessary for accurate scientific observation is impossible. As an art its success depends primarily on the values expressed, in words or deeds, by the therapist, and only secondarily on the use of techniques based on scientific knowledge. Nevertheless all those interested in this subject will welcome the report of the group Psychotherapy research project of the U.S. Veterans Administration. The team engaged in the research is a large one comprising 24 medical doctors (of whom 10 were psychiatrists and the rest psychiatric residents), 5 clinical psychologists and 2 psychiatric social workers. Not only were group methods used for neurotics, but they were also tried for chronic schizophrenics who had not responded to other forms of treatment. By using a clinical psychologist or social worker as an observer at the groups an attempt was made to observe and evaluate the therapist's behaviour as well as that of the patients. The aim of all those taking part in this project was to limit themselves to one method of therapy best described as analytic in orientation. Detailed accounts are given of many group situations and the different ways of dealing with them adopted by the various therapists, and the general conclusions which were drawn by the team as to the efficacy of these different methods. It is obvious that a great deal of work has been done, and if as yet no very definite facts and conclusions have been drawn this is due to the great complexity of the problem, and to the difficulty of noting and recording the innumerable factors involved in group interactions, and determining which of them are significantly related.

E. L. HUTTON.

Rorschach's Test. 1. Basic Processes. By SAMUEL J. BECK. George Allen & Unwin, 1950.

The value of projective techniques lies in the fact that the test material evokes a unique pattern of response from each experimental subject, thereby revealing those unique qualities which are the distinguishing marks of personality. This same fact however also provides the greatest difficulty in the use of these tests for it provides no fixed standard by which to judge each person's performance. The only way in which this difficulty can be overcome is by the comparison of a large number of records, and the compilation of statistical data, and this valuable service has been carried out by Beck during the years since Rorschach published his original figures in 1921. The results of his work are published in the present edition, which differs from the earlier one published in 1944, in that it "rests on a much more solid foundation of quantitatively derived norms". For all those using the Rorschach test this is an extremely valuable reference book. For those unfamiliar with the test its value is somewhat lessened by the fact that Beck uses a system of scoring symbols which differs considerably from that used by the majority of workers in this country, based on the scoring system of Klopfer and Kelly. Not only does he use different letters for the same category, but certain categories are omitted altogether. Thus where Klopfer and Kelly use FK., K.F. and k for shading responses Beck uses FV. and Y. and where the former uses c for texture Beck uses T. This seems particularly unfortunate in view of the fact that the importance of these categories was realized and scoring symbols devised by Binder and Klopfer and Kelly before Beck introduced his own. Beck also entirely rejects the two categories of animal and inanimate movement, FM. and m. thus

following closely the practice of Rorschach and Oberholzer. Everyone who uses the Rorschach test must decide for himself which scoring system he is going to adopt, but the limitation of movement response to anthropomorphic movements does seem to lead to considerable difficulties, and Beck himself says that in scoring certain abstract or inanimate movements as M. he does so "frankly as an act of faith in Rorschach and Oberholzer rather than from conviction based on validated findings".

This book will have to be judged on conjunction with the second volume in which Beck proposes to treat his methods of interpreting the data based on the statistical norms.

E. L. HUTTON.

The Psychoses of Passion (Les Psychoses Passionnelles). By J. BOREL. L'Expansion Scientifique Francaise, Paris (no date).

Pathological passion is not a nosological entity, but a symptom occurring in a variety of psychotic conditions, most frequently, according to the author, in manic-depressive and paranoid psychoses. It has, however, its own pathogenesis: irregularities of cerebral organization due to heredity and constitution are responsible for "dystonia" of temperament and "dystrophia" of character which represent the fundamental psychopathological features. Types distinguished are the querulatory and the vindictive type, hypochondriasis, passion of jealousy and erotomania. The querulatory and vindictive types arise from a clash between their "*tendances excessives*" and their social environment and are characterized by momentary exaltation of affect. Hypochondriasis is the anxiety of the paranoiac; if the hypochondriac believes his physical complaints are caused by somebody else, he is annoyed, protests and asks for vengeance and becomes thus a querulant. There is always both a paranoic and a cyclothymic element present in hypochondriasis, one or the other may prevail. The passion of jealousy may present itself as reactive, but its fundament is always a character anomaly; as a character trait it carries conviction; but if it is based on anxiety arising from fear of infidelity and hyperemotion it is easily turned into doubt. The character abnormality is also fundamental in erotomania: "Everybody gives his proper character in love."

Passion is considered a morbid "neoformation" which severs the ideo-affective relations between patient and his social environment; it creates an entirely subjective psychology and the rapport with the objective world becomes an illusion. The passionate maintains the continuity between past and future by his impulsive tendencies. Superficially the patients may appear imaginative, but in fact there is a poverty of thought. In their conduct the passionates are rigid, hyperemotional, categoric and untruthful.

This is an interesting and original attempt to abstract pathological passion from the various psychotic settings in which it occurs and to establish a common psychopathology and pathogenesis. The analysis of the problem is carried out in the consequent and persuasive manner so characteristic for French writers. There are a number of interesting case records and the literature on the subject is widely discussed. One can criticize the use of certain rather ill-defined terms which has its particular difficulties for the English reader. The author concludes his study with a plea for better knowledge of those emotional states which one only can signify by the name of "*états passionels*".

R. KLEIN.

Psychotic and Neurotic Illnesses in Twins. By ELIOT SLATER, with the assistance of JAMES SHIELDS; statistical appendix by JOAN MAY. Medical Research Council, Special Report Series, No. 278. London: Her Majesty's Stationery Office, 1953. Pp. 385. 21*s*.

The book is an account of 295 pairs of twins one of whom had, for some reason, shown mental or neurological abnormality. It is largely factual in content, providing the data on which any scientific knowledge of the aetiology of mental illness must be based.

It can unhestitatingly be recommended, and will undoubtedly be an authoritative source for many years to come.

W. ROSS ASHBY.

Introduction to Clinical Neurology. By Gordon Holmes, M.D., F.R.S. Second Edition, 1952. Edinburgh and London: E. & S. Livingstone Ltd. Pp. 189. Price 12*s.* 6*d.*

This edition differs little from the first apart from the fact that the author has "allotted more space to a few other subjects as the hypothalamus". When we turn up this we find a very brief account of a subject which might well have had a whole chapter devoted to it even in such an "introductory" book as this is. The book, which is a good one, might gain considerably in value by being expanded to twice its present size. G. W. T. H. Fleming.

Hypnosis in Medicine. By A. Philip Magonet. London: William Heinemann, Medical Books, Ltd., 1952. Pp. 104. Price 9*s.* 6*d.*

The author, who is President of the Medical Hypnosis Association, describes simply and clearly the technique and phenomena of hypnosis. This takes twelve pages.

Most of the rest of this earnest little book is devoted to medical case histories of obstetrics, psychosomatic disturbances and psychoneuroses. These are developed on usual psychiatric lines except that pertinent points in the history are elucidated or the interpretation is made with the patient in a trance.

"She was a good subject for hypnosis and was soon in a deep trance. I explained to her the real causes of her symptoms . . . The patient was better from the time she woke up."

The whole thing seems so simple and successful. Dr. Magonet uses hypnosis as an aid to normal general practice, and yet one is still not convinced.

There is nothing indeed mysterious about this book's presentation of the case, but the hypnotic state itself appears still to be mysterious. Perhaps it is this which cautions so many doctors against its use.

By what hybrid of the instincts is this curious phenomenon of extreme suggestibility and uncanny rapport produced? One is not impressed by the explanation that "hypnotic phenomena are nothing more than conditioned reflexes".

One hopes that hypnotism, being "now the subject of exact scientific enquiry all over the world", will yield its secret. Perhaps another edition of this book will have more to say on the fundamental nature of the hypnotic trance.

The bibliography also should be completed: one reference in the text is merely to "a recent medical paper"; and in several instances even that degree of reference is omitted. C. E. H. Turner.

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Studies on Headache

Cranial-artery pulse waves were recorded two to five times a week from 75 migraine subjects. More than 5,000 samples were assembled of cranial-artery pulse-wave tracings taken at various intervals prior to, during, and after migraine headache attacks. Seventy-two cranial-artery pulse-wave records were also obtained from 10 subjects who seldom or never had had headache and who did not have headache during the three months' period of observation.

One hundred consecutive right-temporal-artery pulse waves recorded from each of 10 headache-free migraine subjects were measured and compared with similar records obtained from 10 subjects who never had headache. From the data the following conclusions were drawn:

1. The caliber of the temporal artery was significantly larger in the headache-free migraine group than in the non-headache group. Also, the caliber during the headache attack was larger than that during the headache-free period, and much larger than that in the non-headache subjects.

2. The migraine group, as contrasted with the non-headache group, exhibited greater variability of the contractile state of the observed vascular bed.

3. In the migraine group the characteristic variability of the temporal-artery pulse-wave contours became more striking about 72 hours prior to the onset of headache and was maximal at the height of the headache attack.

4. The pulse-wave contour changes associated with the headache attack merely punctuated a more or less continuous physiological process and may be viewed as part of the life adjustment of these persons.

(Authors' Abstr.)

Factors that Influence Prognosis in Acute Focal Cerebrovascular Lesions

A study was made of 223 patients who had acute focal cerebrovascular lesions and who were observed at the Mayo Clinic during a period of two years. Of the entire group of patients, 82·5 per cent. had cerebral infarction without embolism, 10·8 per cent. had cerebral embolism accompanied by infarction, and 6·7 per cent. had focal intracerebral hemorrhage.

Factors that influenced the prognosis in these patients were age; existence of hypertension or cardiac disease or both; speed of onset of the symptoms, and whether the lesion was simple infarction, embolism, or hemorrhage.

Injection of procaine into the stellate ganglion did not appear to influence the prognosis.

(Authors' Abstr.)

Some Relationships of Intelligence, Mental Efficiency, Mental Deterioration and Disease

There were marked mean age differences among the various disease groups.

There also were differences among the disease groups in the amount of education completed.

A rank-order coefficient of correlation between age and education of −0·73 indicated that the younger disease groups tended to have more education than the older disease groups.

The mean I.Q.s of nine disease groups and a total hospital group of 668 patients were determined. The mean I.Q. for the total group was 109·0.

A rank-order coefficient of correlation of −0·45 between intelligence and age indicated that the younger disease groups tended to have the higher mean I.Q.s.

A rank-order coefficient of correlation of 0·73 between intelligence and years of schooling completed indicated that the disease groups with the higher mean I.Q.s tended to have the most schooling.

Differences in mean intelligence were found among the various disease groups tested. Fifteen differences in mean I.Q. among the various disease groups were statistically significant at the 5 per cent. and higher levels of confidence.

The postpoliomyelitis, psychoneurosis, and tuberculosis groups had the highest mean I.Q.s, while the amputation, orthopedic, and ulcer groups had the lowest mean I.Q.s.

A separate analysis of approximately 500 test scores on the California Mental Maturity test was made of all the groups studied.

Percentages of mental efficiency and mental deterioration were determined for each of the disease groups. Three disease groups—arthritis, psychoneurosis, and ulcer—had more than 10 per cent. mental deterioration, suggesting the presence of significant organic damage or disorganization.

A rank-order coefficient of correlation between intelligence and mental deterioration was −0·65, which indicated that the groups with the lower mean I.Q.s tended to have more mental deterioration.

A rank-order coefficient of correlation of 0·27 between mental deterioration and age was found and a coefficient of 0·12 between mental deterioration and years of schooling was found.

It was concluded that persons with psychoneurosis and tuberculosis who also have high intelligence are more likely to seek and obtain prolonged treatment. There was no evidence that high intelligence leads to tuberculosis or psychoneurosis. There was some evidence that poliomyelitis patients of high intelligence tend to overwork and become excessively fatigued. Such a condition may be a factor leading to poliomyelitis infection.

Jobs requiring hard physical work and danger are often held by men with low I.Q.s and little schooling. Such men are more prone to have accidents. Low I.Q.s together with the elements of hard labor and danger, may be factors in creating accidents which lead to amputation and orthopedic disabilities.

(Author's Abstr.)

Pituitary-Adrenal Cortex Reactivity in Schizophrenic Patients

A review of the controversy about the reactivity of the pituitary-adrenal cortex system in schizophrenic patients is presented.

The project reported here—set up for statistical evaluation of this reactivity—is outlined.

The results of this investigation would tend to add weight to the conclusion that the reactivity is not impaired in schizophrenia.

It is confirmed that a number of nonspecific stress factors influence the level of pituitary-adrenal cortex activity.

The presence of false-negative responses in any evaluation of the pituitary-adrenal cortex system is emphasized.

Fasting and bed rest do not appear to have an important influence on the activity of this system.

Epinephrine in large doses loses its specificity.

Speculation about the refractoriness of the pituitary-adrenal cortex system is offered.

Electroshock therapy, both convulsive and subconvulsive, exercises a specific influence on the pituitary-adrenal cortex system.

Relative eosinophilia in schizophrenic patients was again found in this population, as has been reported by other authors.

(Author's Abstr.)

Hallucinations in Braille

The case is reported of a young woman who, many years after the onset of blindness, had a schizophrenic reaction with hallucinations of hearing and of seeing. The visions were predominantly in braille. The hallucinations disappeared immediately after unilateral amygdaloidectomy. Suggestions are made as to the motor component of hallucinations and their similarity to the sonar mechanism employed by Cetacea and Chiroptera for the purpose of orientation.

(Authors' Abstr.)

Effect of Carbon Tetrachloride on the Nervous System

Carbon tetrachloride is a common household article whose danger as a potentially lethal intoxicant has not been advertised sufficiently. Labeling of the container should be similar to that for other poisons, and the public should be educated regarding the deadly potency of the fluid. A single exposure can be fatal.

Alcohol imbibed during exposure greatly increases the toxicity of carbon tetrachloride, a fact that should also be better known.

Acute carbon tetrachloride poisoning is dominated by symptoms of the central nervous system, such as headache, diplopia, incoordination, paresthesias, impaired vision, confusion, and coma.

An etiological classification is tabulated.

Reports of neurological aspects of carbon tetrachloride intoxication are extremely meager, incomplete, and scattered.

A total of 15 cases of carbon tetrachloride poisoning are reported and typical ones cited. Neuropathological findings are described, and the literature is reviewed.

(Authors' Abstr.)

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Hippocampal Seizures and Their Propagation

Weak electrical or mechanical stimulation of the fimbria hippocampi in cats induces motor fits and electrical discharges with characteristics having some similarity to those of psychomotor epilepsy. These discharges are not propagated through the fornix but spread through the commissural fibers of the psalterium to the temporal lobe and other parts of the cerebrum. The thalamus and hypothalamus are not essential in this propagation.

(Authors' Abstr.)

Figure-Ground Discrimination and the "Abstract Attitude" in Patients with Cerebral Neoplasms

Forty patients with neoplasms of the cerebral hemispheres were tested on a modification of Gottschaldt's figure-ground visual discrimination, a Weigl type of sorting test, and the Wechsler-Bellevue Form 1. Twenty-four patients with either increased intracranial pressure of unknown origin or spinal cord tumors were used as control subjects. Results show that the group of patients with hemispheric lesions were significantly inferior in their performance on all tests to the control group. Individual patients, with or without cerebral damage, varied within wide limits on all the tests precluding any simple interpretation of a qualitative change in performance after a brain lesion. No significant differences between patients with pre- or post-Rolandic lesions could be found. These results indicate that "intellectual" deficits may be produced by lesions in any portion of the cerebral hemispheres, and not chiefly by frontal lobe involvement, as some authorities are still claiming. More adequate testing methods are needed to aid in the definition and solution of the problem of intellectual functioning and brain injury.

(Authors' Abstr.)

Syringomyelia

Eight cases of syringomyelia are presented with necropsy. Some patients were observed for as long as 20 years. The course frequently is stormy for a few months or years, and the disease then becomes quiescent or only slowly progressive. Intramedullary neoplasms of the spinal cord constitute the chief diagnostic difficulty. Many types of sensory dissociation may be encountered in syringomyelia. In addition to the commonplace loss of pain and temperature sensation with preservation of touch; heat and cold sensation, pain and temperature sensibility, and vibratory and position sensation may be dissociated. There was loss of vibratory sensation with intact position sense early in the course in six of eight cases. Evidence is presented to show that pallesthetic fibers may not be situated in the posterior columns, but, rather, may lie in the medial portion of the lateral columns.

Treatment of the disease is wholly unsatisfactory. There have been no controlled experiments to determine the value of X-ray therapy or of surgery. The symptomatic improvement occasionally obtained may well be psychogenic. X-ray therapy lacks a rationale and, indeed, may be harmful.

It is shown that the central canal of the adult cord frequently is the site of a disorderly proliferation of ependyma. This contrasts with the single layer of epithelium found in the infant. It is concluded that such ependymal proliferation is an acquired variant rather than a congenital rest. Current ideas of the pathogenesis of syringomyelia are discussed, and a general theory of the pathogenesis of the disease is offered. This theory relates the developmental origin of the disease to anomalies of the intramedullary blood supply. When the patients reach adult life, vascular insufficiency and occlusions lead to cavitation, gliosis, and fibrosis. The theory is considered in relation to, and accords satisfactorily with, the clinical data, the location of the lesion, the pathologic findings, and the common association of this disorder with intramedullary hemangioblastomas.

(Author's Abstr.)

Autonomic Responses in Differential Diagnosis of Organic and Psychogenic Psychoses

Patients with cerebral damage show striking inability to learn conditional responses, which normal subjects learn regularly and promptly.

The patients, who had severe, diffuse cortical impairment, uniformly failed (within 6 to 23 reinforced stimulations) to establish discriminative conditional responses to visual stimuli associated with a slightly painful electrical stimulus. The types of reaction which were recorded include skin resistance, respiratory movements, heart rate, spontaneous and integrated motor movements (tremors and gross movements), and verbal formulation. In none of these forms of behavior did the brain-damaged patients show any formation of conditional responses. This is in marked contrast to responses of the normal subjects, who, after two to seven reinforcements, invariably showed evidence of conditioning. In the normal, the evidence of conditional response formation was always present with integrated motor responses and in verbal formulation, and usually in the psychogalvanic reflex.

In the human subject, changes in heart rate in relation to conditional reflex formation are much less marked than in comparable experiments on dogs. Clarification of this difference awaits more refined study.

(Authors' Abstr.)

Eosinophile Response in Schizophrenic Patients

The changes in level of circulating eosinophiles in both morning and afternoon control periods and in response to epinephrine (0·3 mg. given subcutaneously) and to corticotropin (25 mg. intramuscularly) were determined in 30 men hospitalized for schizophrenia an average of 8·5 years.

The mean changes in eosinophile level observed in the control periods reflect the diurnal cycle of eosinophile level previously described. The mean relative decreases in eosinophiles following administration of epinephrine or corticotropin were less in the afternoon than in the morning. The relative amount of fall apparently depends upon the coincident direction of the spontaneous diurnal cycle as well as upon the health of the adrenocortical system.

The number of schizophrenics showing a fall of 50 per cent. or greater to epinephrine (13/30) or to corticotropin (18/30) in the morning was smaller than would be expected in a group of healthy men.

Of the 30 schizophrenics, 11 had been classified as catatonic and 12 as paranoid. The results in these two groups showed distinct differences.

The catatonics showed relatively normal responses to epinephrine and corticotropin but decreases greater than normal on the control morning. The paranoids produced significantly smaller responses to epinephrine and corticotropin but normal eosinophile changes in the control periods.

The mean absolute level of circulating eosinophiles in the catatonics was similar to that in normals, whereas that of the paranoids was twice as high.

It is concluded that these eosinophile studies provide presumptive evidence that the adrenocortical system is hypoactive and hyporeactive in the paranoid schizophrenic and perhaps hyperreactive in the catatonic schizophrenic. This may explain the conflicting reports on adrenocortical function in schizophrenia.

(Authors' Abstr.)

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An Electroencephalographic Study of Barbiturate Anesthesia

1. A series of changes in the EEG brought about by intravenous injection of sodium amytal were described.

2. The characteristic fast waves caused by intravenous injection of sodium amytal were roughly classified into FA of about 15 c/sec. and of relatively large amplitude, and FB of relatively small amplitude, the frequency of which is around 25 c/sec. or over.

3. When a stimulus is applied in a stage of anesthesia, especially during emergence from anesthesia, there appears a EEG pattern which would correspond to a more light stage of anesthesia. At that time the behavior shown by FA and FB seems to be analogous to the behavior of alpha and beta waves at the time of non-anesthetized case (awaking period and during natural sleep).

4. In instances where slow waves are present before anesthesia, the slow waves appear in response to stimulation at the time when anesthetized normal subjects show alpha waves or FA.

5. No fast waves can be elicited by administration of sodium amytal in certain stages of insulin hypoglycemia, immediately after electrically induced convulsions and in deep anesthesia etc., when the brain function is disturbed above a certain degree. As the functional stage of the brain recovers due to administration of glucose or spontaneously with the lapse of time the fast waves which could not be seen before appear very clearly. (Authors' Abstr.)

The EEG Effect of Metrazol and Photic Stimulation in 682 Normal Subjects

This paper describes some exploratory experiments, designed to test certain aspects of the well-known hypothesis that "scanning" of the visual field takes place at the frequency of the alpha rhythm. A rectilinear pattern was produced electronically on an 18-inch C-R tube screen, and modulated rhythmically in size at frequencies between 2 and 30 per sec. No "stroboscopic" effects, such as might have been expected on the scanning hypothesis, were observed by the subjects tested.

In later experiments the subject's EEG was simultaneously recorded, and a simple correlator used to indicate the phase-relation between the size-modulation and the dominant component of the occipital and other potentials. With the eyes open no significant correlation was observed even when the occipital EEG was fed back to control the brightness of the modulated pattern.

Although the results cannot be said to disprove the scanning hypothesis, they appear to circumscribe the role attributable to the alpha rhythm in such speculations.

(Authors' Abstr.)

Some Cerebellar Effects on the Electrocorticogram

The present study was made on cats maintained under d-tubocurare or di-hydro-beta erythroidin.

1. Cerebellar stimulation can alter the electrical activity of both sensory and motor areas of the cerebrum.
2. Changes in cerebral activity following cerebellar stimulation usually indicate more pronounced "activation" patterns; rarely, slow waves and spindles follow such stimulations.
3. Localized areas of the cerebellum can influence localized cerebral areas.
4. Possible relationships of the cerebellum to the diffuse activating system is discussed.

(Authors' Abstr.)

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Further Analysis of the Temporal Lobe Syndrome Utilizing Frontotemporal Ablations

1. Ten subjects, 1 adult male Chacma baboon, 1 adult female Guinea baboon and 8 immature rhesus macaques were used. One baboon and 5 macaques received extensive bilateral ablations of the frontotemporal region of the cerebral hemispheres as defined in neuronographic studies. The additional animals received lesions restricted to the orbital, insular, and temporal portions of the region. Locus and extent of lesion was verified histologically and reconstructions were made. Thalamic degeneration was analyzed.

2. A battery of observations and tests was administered pre- and postoperatively. This battery included such tests for visual processes as determination of the extent of visual fields, examination of visual pursuit and visual acuity, training for performance of visual pattern discrimination and testing of discrimination of food from non-food objects. Acceptance thresholds for quinine solutions of various concentrations were determined. The response to social and noxious stimuli was recorded. Performance of delayed response was tested. Locomotor activity, food intake, and basal temperature determinations were made, and sleep-activity cycles observed.

3. In general, reconstruction showed lesions to be bilaterally symmetrical and to include most of the cortex of the posterior orbital gyrus, anterior and limen insulae, as well as temporal pole, periamygdaloid cortex and amygdala. Degeneration in the medial magnocellular portion of the n. medialis dorsalis, midline intralaminar, n. medialis ventralis, and medial pulvinar of the thalamus were related respectively to the lesions in the posterior orbital gyrus, anterior perforate substance and limen insulae, temporal polar formations, and anterolateral temporal cortex.

4. Several aspects of the complex syndrome associated with large bilateral temporal lobe lesions were selectively related to interference with the frontotemporal region. Performance in vision, with respect to acuity, extent of field, and ability to make discriminations was unaffected by such lesions. No changes with respect to ability to localize tactile stimuli were observed. Range of movement was unaltered. Performance in the delayed-reaction test was unimpaired. On the other hand, altered behavior did occur in the categories of taste, anergy metabolism and approach to or avoidance of a variety of stimuli including noxious and social ones.

5. This specificity of results takes on added significance in light of the fact that ablation of adjacent regions of the frontal and temporal lobes have produced a different constellation of behavioral changes. Ablations in the lateral frontal region are associated with selective interference with delayed-response-type functions (Pribram, Mishkin, Rosvold and Kaplan, 1952). Inferior temporal ablations result in selective impairment of animal's ability to solve simultaneously presented problems of visual discrimination (Chow, 1951; Mishkin, in press; Mishkin and Pribram, in press).

6. Further subdivision of the syndrome is possible by making more restricted lesions in the frontotemporal region. Specifically, the frontal portion of the region is related to locomotor activity, the insular portion to taste, and the temporal polar-amygdaloid formations to food intake and temperature regulation.

7. The relation between altered appetitive mechanisms related to metabolism and altered reaction to noxious and social stimuli is pointed out.

(Authors' Abstr.)

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Clinical Hypothalamic Syndromes

In this paper attempt has been made to describe one clinical hypothalamic syndrome which is characterized by a certain type of coma previously alluded to as coma vigil. In this state of coma the individual may keep his eyes open, the eyeballs may wander, and he may give the impression that he is awake and in contact with his environment, though he is not. Generally there are no focal signs and there is no evidence pointing to other regional involvement of the brain. The patient may be extremely restless and give evidence of sexual excitement or general psychotic behavior. In addition, there may be and often are one or more signs or symptoms reflecting disturbance of function of the diencephalon. Among these are fever, often high, not the result of infection. There may be hypothermia. If fever is present it is unaccompanied by its usual manifestations. There is want of parallelism between fever and pulse rate, the latter often being low when the former is high; that is, there is dissociation between them. The fever may respond to barbiturates when it does not to antipyretics. There may be excessive, indeed extremely profuse, perspiration in the absence of fever. The blood pressure may drop to normal or below in known hypertensives or fluctuate in either direction in individuals who were known to have normal blood pressure. There may be polyuria, transient glycosuria and hyperglycemia in nondiabetics. Occasionally one observes minor twitchings, at times a major convulsion.

The condition may occur on the basis of vascular disease or infections, often an encephalitic process. It may be the result of trauma to the brain, especially of the base. It may be one aspect of other pathologic processes, more particularly tumors, which impinge on the interbrain region. The syndrome may occur in the course of tumor of the third ventricle, craniopharyngioma, or other neoplasms at the base in the middle fossa. It may occur in the course of diabetic or other encephalopathy. The condition is always grave and frequently ends fatally. It may end in recovery, in which case, if the pathologic process was limited to the hypothalamus, there need be no residua. The coma may last days, weeks, or months and end either in death or in recovery.

Several minor diencephalic syndromes have been alluded to, namely diabetes insipidus, behavior disorders, variations in states of consciousness, fever of unknown origin, and petit mal seizures. The latter may be characterized by extreme pallor, drop in blood pressure, and rise in pulse. This type of petit mal may be favorably affected by ephedrine or dexedrine and not by sedative anticonvulsants; sometimes a combination of the two may be effective when neither alone is.

The paper includes a brief summary of the anatomy of the hypothalamus, of its numerous afferent and efferent pathways their connections with other parts of the brain, and of the blood supply. Extensive consideration is given to the neurophysiology of the hypothalamus, including discussion of the metabolic functions of the interbrain structures and their relationship to states of consciousness and to mental and emotional disturbances.

This being a clinical study, evidence of pathology was purposely left out, not because it is unimportant. Attempt has been made to correlate clinical observations with regional anatomy and experimental physiology and pathology. Symptoms were interpreted in the light of what is known so far of the normal function of the hypothalamus and of the manifestations resulting from experimentally induced lesions or from stimulation experiments. Further studies may throw light on the correctness of the observations and the validity of the conclusions.

(Author's Abstr.)

Suicide in a State Hospital for the Mentally Ill

1. The incidence of suicide among the total admissions at Eastern State Hospital has been noted and it was found that the rate is many times higher than among the general population. While the rate of suicide among the general population was 11·2 per 100,000, the rate at this institution during its entire existence was 38 per 10,000.

2. The highest incidence occurred in the age group of 45-54 years, which corresponds with the findings among the general population.

3. The highest rate of suicide occurred within the first three months of hospitalization, while few patients committed suicide after they had been institutionalized five years or longer.

4. Fifty per cent. of the patients who committed suicide were classified as schizophrenia, while only 10 per cent. were diagnosed as manic depressives, depressed, and furthermore depression was found to be present in only 55 per cent. of the patients, while in 45 per cent. there was no evidence of depressive features, either during the psychotic episodes or in the premorbid personality make-up. Suicide in these cases probably occurred as a result of auditory hallucinations and delusions.

5. The incidence of suicide was then considered during the preshock era and during the shock era. The rate during the preshock era was 42 suicides per 10,000 admissions, while during the shock era it was 32 per 10,000 admissions. However, it was felt that rather than the application of shock treatment, this slight decrease in the suicide rate during the shock era is due to other factors, the most important of which are: (1) the shifting of the average age of the total population to the older age group (during the preshock era 15 per cent. of the admissions were 65 years of age and older, while this increased to 27 per cent. during the shock era); (2) 50 per cent. of the patients were diagnosed as schizophrenics while only 10 per cent. would fall within the manic depressive group; (3) the long duration of mental illness in most of the patients, and finally (4) the fact that depression was at work in only a little more than half of the patients. (Authors' Abstr.)

Improvement in Psychosis Following Conditioned-Reflex Treatment for Alcoholism

1. Five hundred and ninety-one patients were treated by the conditioned reflex treatment for alcoholism.

2. Twenty-seven patients suffered from mental disorders.

3. Of the 27 patients, 21 suffered from mental disorders due to alcohol or associated deficiency states. These patients were divided as follows: 6 cases of delirium tremens, 6 cases of acute alcoholic hallucinosis, 1 case of pathological intoxication, 2 cases of chronic mental deterioration in which there were also alcoholic convulsions, 6 cases of prodromal symptoms of delirium tremens, but in which delirium tremens did not develop.

4. Six patients suffered from mental disorders not due to alcohol. Three of these were cases of involutional melancholia and 3 of schizophrenia, paranoid type.

5. Marked improvement from aversion treatment was noted in all patients except one. This was a case of chronic mental deterioration. In the 3 cases of involutional melancholia and the 3 cases of schizophrenia, paranoid type, unexpected remissions occurred which could not be accounted for by the removal of alcohol alone.

6. Aversion treatments for alcoholism apparently have an unexplained beneficial effect on mental abnormality. It is surmised that this may be due to improvement in cerebral circulation and to physiologic stimulation of the diencephalon and adjacent cerebral centers. (Authors' Abstr.)

The Use of Mebaral in the Treatment of Chronic Alcoholism

Mebaral (tri-methyl derivative of phenobarbital) has been given to 41 chronic alcoholics for the purpose of relieving their tension and irritability and thereby reduce their inclination to drink. In the alcoholic who is tense, restless, insomnic, and constantly agitated, this medication has its greatest benefit. The drug was selected because of the minimal amount of drowsiness or euphoria produced and the lessened likelihood of habituation. All of the patients treated were indigent. Ninety-three per cent. had failed on one or more other forms of treatment, and all had been unable to work steadily for from three to nine years because of their excessive alcoholism.

Difficulty was experienced in maintaining these patients on the medication following their recovery from a bout. In no instance in this series did a patient resume his alcoholism while taking the medication in the prescribed manner. Fifteen have continued to abstain from two weeks to five months. Sixteen were maintained for two to four weeks as out-patients without taking any alcohol, while waiting to begin treatment with TETD (Antabuse). Eleven were unimproved. Eighteen patients on B complex vitamin therapy showed 13 per cent. fewer improved than in the group who also received Mebaral. Those who could be maintained on the drug were able to continue to abstain from the use of alcohol. (Authors' Abstr.)

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Alzheimer's Disease: A Clinico-pathologic Analysis of Twenty-three Cases with a Theory on Pathogenesis

Histochemical and quantitative histological studies of twenty-three cases of Alzheimer's disease suggests two possibilities with regard to pathogenesis of the syndrome and to histogenesis of the lesions. The first possibility and the one that seems to be more likely, is, that it may be due to a disturbance in the cerebral metabolism of iron, resulting in secondary devitalization of the microglia. The second possibility is that there is a primary devitalization of the microglia which leads to the gradual accumulation of metabolic wastes in the nerve and macroglial cells producing their ultimate degeneration.

In either case, the histogenesis of Alzheimer neurofibrillary degeneration and argentophilic plaque formation is believed to be due to microglial insufficiency, whether the latter phenomenon is primary or secondary. The histogenetic theory of microglial insufficiency or inhibition accounts for the origin of plaques from nerve cells as well as from the macroglial and microglial cells. It affords a rational explanation for the apparent dissociation between plaques and Alzheimer cell changes. Depending upon the relative functional state of the microglia, the quantitative relationships between the two related phenomena will vary accordingly from case to case and even in different parts of the same brain.

From a study of an Alzheimer diseased brain six days after cerebral biopsy had been performed, it was concluded that the microglia in the tissue adjoining the biopsy lesion exhibited adequate ability to carry on the complex activities of phagocytosis and of fat elaboration. This suggests that the microglial defect might be one of inhibition rather than of devitalization.

The effects of anti-reticular cytotoxic serum in three cases of Alzheimer's disease were inconclusive but they indicated that the microglial cells, as part of the reticulo-endothelial system, may have been responsive to the stimulation of A.C.S. Further studies along these lines, are indicated.

Significant clinical, pathological and histochemical differences between Alzheimer's disease and senile dementia justify the conclusion that Alzheimer's disease is a metabolic syndrome which may occur independent of senile changes. There is no conclusive evidence that Alzheimer's disease is a premature form of senescence even though it occurs predominantly during the so-called pre-senium.

Expert investigation along biochemical lines is indicated by the foregoing findings and probably until this is undertaken, the solution of the pathogenesis of Alzheimer's disease will remain a mystery. (Author's Abstr.)

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The Brain-stem Lesions in Parkinsonism

The pigmented cells of the brain-stem, especially those in the substantia nigra and locus coeruleus, have been examined in 19 cases of idiopathic paralysis agitans, 10 cases of Parkinsonism with a history of an attack of encephalitis between the years 1918 and 1924, and five cases of Parkinsonism of uncertain aetiology. Five types of changes were found in these cells (1) Saccular distension by lipochrome granules along with disappearance of Nissl granules, melanin, and nucleus; (2) vacuolation, which was considered unimportant; (3) binucleated nerve cells, which were very rare; (4) Lewy's spherical concentric hyaline inclusions; (5) neurofibrillary tangles, somewhat similar to those seen in Alzheimer's disease, but unaccompanied by senile plaques.

The first three types were seen in post-encephalitic cases and in occasional cases in the control group. Lewy's hyaline inclusions were found in all of our cases of typical idiopathic paralysis agitans, and in one complicated case which may have been post-encephalitic. Neurofibrillary tangles were found in nine post-encephalitic cases, in one case associated with amyotrophy, which was clinically idiopathic. In one case of Parkinsonism associated with olivo-ponto-cerebellar degeneration, and in 22 cases in the age group 50 to 90 years, with no signs of Parkinsonism, neither of the last two types of cell change could be found in the pigmented cells of the brain-stem. The significance of these findings is discussed in relation to the literature on the subject. (Authors' Abstr.)

Substances which Support Respiration and Metabolic Response to Electrical Impulses in Human Cerebral Tissues

Human cerebral tissues removed during operations for prefrontal and temporal lobectomy afforded about 40 specimens for determining the initial respiratory rate in a phosphate-buffered saline with glucose as substrate. The mean rate so obtained was of 55 μ moles O_2/g. fresh tissue/hr. The variation in respiratory rate was relatively large (S.D. 10·6) but rates were not systematically different in tissue from frontal and temporal areas. The rates changed little if at all during the first two hours' metabolism.

Applied electrical impulses increased respiration to up to 110 μ moles O_2/g. hr., which is close to the probable respiratory rate of human cerebral cortex in situ.

Aerobic accumulation of lactic acid with glucose as substrate proceeded concomitantly with normal respiration and at about 25 μ mole/g. fresh wt./hr. This also could be doubled by applied electrical impulses.

The respiratory rate of human cerebral tissue in a phosphate saline without substrate was lower initially than when glucose was present and fell further after 30 minutes' metabolism. Electrical impulses effective with glucose were then without action. Fumarate as the only substrate was without effect on the lower rate, on the fall in rate, and on the rate with applied impulses.

Succinate as the only substrate maintained respiration without permitting response to impulses. Citrate maintained less stable rates which were affected little by impulses. Lactate and pyruvate maintained well the respiratory rate of the tissues and permitted clear responses to applied impulses. Reaction to these substrates is similar in human tissues and in those from experimental animals.

With glutamic acid as substrate, human tissues behaved differently from those from other animals examined. Respiratory rate was maintained and responded to applied impulses.

Comparative observations were made on normal and treated guinea-pig tissues and on two specimens from rhesus monkey. (Author's Abstr.)

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Exteroceptive and Proprioceptive Ascending Impulses in Pyramidal Tract of Cat

1. By means of the evoked potential method the existence of the anatomically demonstrated ascending fibers in the pyramid of the cat (4) has been confirmed.

2. The electrical activity set up in the pyramidal tract fibers by an afferent volley from various cutaneous and muscular nerves consists of several positive deflections followed by a low-voltage negative wave. The responses to stimulation of cutaneous nerves are considerably larger than those evoked from muscular nerves and show more distinct deflections, suggesting the presence of groups of fibers of different conduction velocities.

3. There are striking similarities between the ascending and descending pyramidal fiber systems. Thus, the majority of ascending fibers, like the descending ones, appears to be crossed; further, the pyramidal response is greater when stimulating nerves of the forelimbs than of the hindlimbs and greater when induced from nerves supplying the distal parts of the limbs than from nerves innervating the proximal parts; the termination of the ascending fibers in the cerebral cortex finally is much the same as the origin of the descending pyramidal fibers.

4. It is estimated that 70-80 per cent. of the ascending exteroceptive impulses in the pyramid travel by direct spinocortical fibers, and the remaining 20-30 per cent. via nuclei of the dorsal funiculi. The proprioceptive impulses to the pyramid seem to be about equally distributed among the two spinal paths.

5. The possible functional significance of the ascending pyramidal tract fibers is discussed. The suggestion is ventured that they are in some way of importance for the coordination of differentiated, skilled movements and further that they may represent the still unknown afferent path in the plantar and abdominal reflexes and in the placing and hopping reactions. (Authors' Abstr.)

Effects of Lesions on Subcortically Evoked Movement in Cat

The authors have produced phasic movement of the contralateral forelimb in anesthetized cats by stimulation of the caudate nucleus, hypothalamus and anterior thalamus. When movement was induced by stimulating the caudate nucleus, it could be abolished by lesions at the base of the brain stem in the mid-line, at the junction of diencephalon and midbrain. These lesions did not seriously affect cortically induced movement. On the other hand, lesions of the medial portion of the cerebral peduncles abolished movement from cortex and subcortex alike.

The results suggest a pathway for movement, distinctive from the cortico-spinal tracts, that originates in or passes through the caudate nucleus. It then proceeds caudad in or close to the internal capsule, assuming a medial position through the diencephalon before swinging laterally in the midbrain to enter the ipsilateral basis pedunculi and continue caudad in the pyramids. (Authors' Abstr.)

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Results of Transorbital Lobotomy in 400 State Hospital Patients

Four hundred cases of transorbital lobotomy are reported; there was marked improvement in approximately one-half of the cases and some improvement in another 25 per cent. of chronically disturbed patients.

The results according to diagnosis are indicated.

It is urged that this type of operation be considered for all chronically disturbed patients.

The economic advantages in the improvement of such a group are stressed.

(Authors' Abstr.)

Effect of Themisone and Phenurone on Electrically-induced Seizures in the Salamander

The behavior of salamanders during electrically-induced seizures is described in terms of an active and an inactive phase. Both Themisone and Phenurone inhibit the violent active phase of a seizure and diminish the duration of the stupor or inactive phase typically found in untreated salamanders. Phenurone acts more slowly but its effect lasts longer than that of Themisone. Themisone, unlike Phenurone, produces a temporary unsteadiness in gait and some sluggishness. (Authors' Abstr.)

Experimental Intraventricular and Intracerebral Injection of Polymyxin B in the Cat

1. Twelve cats, including three controls, were used in this experiment.

2. In four cats, 2,500 or 5,000 units of polymyxin B in 0·05 cc. of normal saline solution were injected into the left lateral ventricle under Nembutal anesthesia. None of these cats showed any toxic neurologic reactions. Sections of the brains of these animals revealed no significant changes.

3. Five cats were given an intracerebral injection of polymyxin B, 2,500 or 5,000 units, into the left cerebral hemisphere. One cat was injected under sodium Nembutal and the other four without anesthesia. Only one animal developed a reaction; sections of the brain showed that the injection was in the left thalamus, internal capsule, and the region of the hypothalamus.

4. Pathologic examination revealed acute inflammatory changes in the leptomeninges and minimal hemorrhage in the early stage of the experiment, and softening and gliosis in the area of the intracerebral instillation in the later stage. (Author's Abstr.)

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Acquired Epilepsy: A Study of 535 Cases

Records of 1,648 patients with a diagnosis of epilepsy were reviewed. Of these, 535, or 32·4 per cent. gave evidence of organic lesion of the brain acquired prior to the person's first seizure. In 52 per cent. the evidence for the pathologic change was believed conclusive, in 48 per cent. only probable. Of the 535 patients, 69 per cent. were private and 31 per cent. clinic patients, the latter being adolescent or younger.

Ninety per cent. of patients had the first seizure before the age of 20; 24 per cent. had a positive family history of epilepsy. Evidence for a cerebral lesion was furnished in largest

proportion, 88 per cent., by the patient's past history, with the electroencephalogram, description of seizures, neurologic examination, and pneumoencephalogram following in order of importance.

Causes of pathologic change were assigned as follows: prenatal 13·3 per cent.; natal conditions 30·1 per cent.; postnatal trauma 20·7 per cent.; infections 17·2 per cent.; other conditions 6·4 per cent.; and unassigned 12·3 per cent.

Data studied with respect to the patient's age at the first seizure showed a progressive decline of paranatal mishaps and progressive increase of postnatal traumatic conditions with increasing age. Nearly one-half of the cases, 46 per cent., had the initial seizure within 12 months after the first etiologic event. In 12 per cent. epilepsy did not arise until ten or more years later. The time interval separating etiology and epilepsy was shorter for postnatal trauma and infections than for paranatal conditions.

The distribution of causes differs radically from a previous series of older patients.

A comparison and coalescence of data from various sources with delineation of genetic and acquired factors is desired. (Authors' Abstr.)

Clinical Evaluation of Pagitane Hydrochloride in Parkinsonism

Irrespective of all the pitfalls of an analysis such as this on a relatively small number of patients, the authors' experience with this compound has allowed them to formulate the following conclusions which are in general agreement with published reports now appearing on the use of Pagitane hydrochloride.

1. This compound is an effective drug in reducing the rigidity and tremor encountered in Parkinsonism.

2. It can frequently be given in larger doses than similar compounds previously available, without producing unpleasant side reactions which would necessitate discontinuing medication.

3. A tendency is noted for some of the patients to report greater improvement soon after beginning therapy. This characteristic of Parkinsonism and makes evaluation of the new remedy difficult.

4. As had been noted previously by others, those patients respond poorly to medical management who have Parkinsonism appearing late in life, in whom tremor is the predominant symptom, and who have been diagnosed as having central nervous system changes attributable to arteriosclerosis. In these patients, mental confusion is frequently produced and the drug, if used at all, must be given with great caution.

5. Best results were obtained in Parkinsonism of idiopathic or postencephalitic etiology. (Authors' Abstr.)

Stimulation of the Amygdaloid Nuclear Complex in Unanesthetized Cats

1. Electrical stimulation of the amygdaloid nuclear complex in unanesthetized cats has elicited complex somatomotor and visceromotor effects: contraversive movements, tonic and clonic movements of the extremities, licking, sniffing, chewing, and inhibition of respiratory and other spontaneous somatomotor activities; pupillo-dilation, salivation, micturition, defecation, and pilo-erection. These responses were obtained mainly from the phylogenetically old anteromedial division of the amygdaloid nuclei which receives fibers from the olfactory bulb and which projects to the septal, preoptic, and hypothalamic areas.

2. Stimulation of the phylogenetically younger basolateral division, which appears to have no direct connections with fibers from the olfactory bulb and whose efferent projections are unknown, produced behavior changes very similar to those obtained by stimulating the hippocampus and the medial prefrontal, limbic, retrosplenical, and hippocampal gyral cortices, indicating functional relationships between all these structures. This response consisted of searching movements to the contralateral side associated with bewilderment and anxiety, and sometimes with fear, anger, and fury.

3. The results are discussed in relation to temporal lobe seizures. It is believed that the amygdala plays an important role in certain types of epileptic automatisms. (Authors' Abstr.)

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Observations on 36 Patients with General Paresis Treated with Penicillin-Malaria and Penicillin Alone

1. Of 36 patients with general paresis, 18 were treated with penicillin-malaria and 18 with penicillin alone.

2. Choice and methods of treatment, as well as complications, were described.

3. The prognosis in the series presented was found to depend mainly on (*a*) duration of symptoms, (*b*) degree of intellectual impairment, (*c*) type of psychosis, (*d*) combination with tabes, (*e*) age. These findings confirm often-reported observations by others.

4. Satisfactory clinical results (much improved and improved) were achieved in 61·1 per cent. (11 patients) treated with penicillin-malaria and 27·7 per cent. (5 patients) treated with penicillin alone. Satisfactory serologic results (available for 33 patients only) were obtained in 94·1 per cent. (16 of 17 patients) in the combined group and in 81·2 per cent. (13 of 16 patients) in the penicillin-alone group.

5. The clinical failure rate was 22·2 per cent. (4 patients) for the patients treated with penicillin-malaria and 38·8 per cent. (7 patients) for the patients treated with penicillin alone; the serologic failure rate was 5·8 per cent. (1 of 17 patients) and 18·7 per cent. (3 of 16 patients) respectively.

6. Some superiority of the combined treatment remains even after allowance has been made for factors rendering the composition of the group treated with penicillin-malaria more

favorable. Penicillin alone, however, outranks the combined treatment with regard to safety, lack of complications, and ease of administration. (Author's Abstr.)

Involutional Melancholia

1. The pre-psychotic personality of patients developing agitated depressions is described as the anal-compulsive character.
2. The development and characteristics of the anal character are outlined.
3. The agitated depressions are considered as the decompensation of an anal character.
4. The precipitating factors are considered to be traumata which prevent the maintenance of characteristically rigid ego defenses.
5. A differential comparison is made of the psychodynamics of the reactive and agitated depressions.
6. The psychopathology of the symptoms is related to the prepsychotic personality and its decompensation. (Authors' Abstr.)

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Investigations on the Disulfiram-Alcohol Reaction

Following the administration of disulfiram (tetraethylthiuram disulfide) and alcohol in various doses to 39 subjects, a reaction with a typical course was found in conformity with the reports of other investigators. In spite of the typical course, great individual dissimilarity was observed.

The symptoms reflect a radical process influencing several organs and systems of organs (the cardiovascular and respiratory systems and the gastrointestinal canal).

The cause is presumably the acetaldehyde formed in the organism but the mechanism is largely unknown.

Tests of cutaneous reaction showed no direct hypersensitivity to alcohol.

The degree of the reaction released is to some extent dependent on the quantity of disulfiram administered. From a therapeutic view-point the administration of large doses has no advantages. (Author's Abstr.)

Hepatic Abnormalities in Alcoholics with Delirium Tremens

1. Aspiration biopsy of the liver in 66 patients with delirium tremens revealed a normal liver structure in 19 (29 per cent.), focal inflammation in 4 (6 per cent.), fatty infiltration in 20 (31 per cent.) and portal cirrhosis in 23 (35 per cent.).

2. Clinical and biochemical liver function studies did not provide a clue to the encountered histology. The dissociation between biochemical tests and histology suggested that the latter was not responsible for the observed liver function changes.

3. Hepatic abnormalities in delirium tremens appear to be due to dietary inadequacies. A diet deficient in lipotropic substances was associated with fatty infiltration and eventually led to fibrosis and portal cirrhosis. The degree of alcoholism and severity of cerebral symptoms could not be correlated with hepatic abnormalities.

4. Rehabilitation of the alcoholic patient is desirable to prevent progressive liver injury. The fatty liver is curable, and prognosis in patients with hepatic fibrosis and portal cirrhosis is improved with treatment. (Authors' Abstr.)

Driving Under the Influence of Alcohol. The Role of Chemical Tests in Appealed Cases

1. The role of chemical test evidence has been evaluated as the result of a study of pleadings, verdicts and dismissals in cases prosecuted for driving under the influence of alcohol.

2. In the cases examined, the concentrations of alcohol in the blood ranged from 0·14 to 0·40 per cent., indicating the consumption of more than ½ pint of whisky or the equivalent amount of other alcoholic beverages.

3. The use of the Alcometer breath test to determine the concentration of alcohol in the blood resulted in a marked increase in pleas of guilty, from 23 to 61 per cent. This increase indicates an acceptance of the validity of the test by defendants, since the test result actually corresponds to what they know they had consumed.

4. There was a significant increase in convictions by both court and juries, from 58 to 83 per cent. This increase results from the confidence reposed by the court and juries in the chemical test and from the value of this test in corroborating other evidence.

5. The cases dismissed by the prosecutor for lack of sufficient evidence decreased from 22 per cent. to none when chemical test evidence was introduced. In addition to the confidence of the prosecutor in the reliability and corroborative value of the chemical test, this decrease results from the more effective screening by the police of cases not warranting prosecution.

6. The over-all rate of convictions rose from 55 to 93 per cent. when chemical test evidence was presented.

7. This evaluation of the disposition of 87 cases brought before the New Haven County Court of Common Pleas reveals the acceptance of the chemical test by all segments of the community as an effective means of convicting the guilty and protecting the innocent. (Authors' Abstr.)

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1. Biochemistry, Physiology, Pathology, etc.

Influence of Various Afferent Nerve Stimuli on the Composition of the Secretion of the Adrenal Medulla in the Cat. Euler, U. S. v., and Folkow, B. [*Naunyn-Schmiedebergs Arch. exptl. Pathol. Pharmakol.*, **219**, 242 (1953).]

Compression of the carotid of cats in chloralose anesthesia produced in the venous blood of the adrenal 0·2 γ noradrenaline (I)/per kg. and min. which amounted to 56 to 90 per cent. (average 72) of the sum of (I) and adrenaline (II). After stimulation of the afferent ischiadicus or plexus brachialis the (I) production was 0·16 γ which amounted to 43 per cent. of the total. After electric stimulation of the splanchnic nerve the percentage of (I) was 73, in asphyxia 78. Conclusion: (I) and (II) are produced by different cell groups which are responding to specific stimuli. A. E. Meyer (Chem. Abstr.)

The Schizophrenic Process; Animal Experiments with C^{14}-Mescaline. Patzig, Bernhard, and Block, Wolfram. [*Naturwissenschaften*, **40**, 13 (1953).]

Review of experiments on feeding mice with radioactive mescaline and determination of the resultant distribution of it in the body. B. J. C. van der H. (Chem. Abstr.)

Strychnine as a Depressant of Primary Inhibition. Bradley, K., and Eccles, J. C. [*Nature*, **171**, 1061 (1953).]

It is demonstrated by experiments on low spinal cats under light nembutal anesthesia that the threshold for stimulation in the quadriceps nerve of group Ia components, which have excitatory action on homonymous motor neurons and inhibitory action on antagonistic motor neurons, is lower than that for group Ib components which have opposite effects. Selection of the proper stimulus permits the application of a nearly pure Ia afferent volley to the motor neurons of the antagonistic biceps-semitendinosus nerve, and the amount of inhibition produced is measured by the height of the reflex spike resulting from a single maximum afferent volley applied at various times following the preliminary Ia inhibitory volley. A subconvulsive dose, 0·09 mg. per kg., of strychnine diminishes and shortens the inhibition, and a further dose 0·08 mg. per kg., virtually abolishes the inhibition. Strychnine seems to have a specific depressant action on synaptic inhibition for this action is observed with doses which have no significant effect on synaptic excitation in a monosynaptic reflex. The action of strychnine in diminishing inhibition is discussed with relation to a postulated inhibitory transmitter substance (Brock *et al.*, *J. Physiol.*, **117**, 431 (1952)) and as an explanation of its convulsive activity. J. A. Bain (Chem. Abstr.)

Migraine as a Psychosomatic Disease. Campbell, Dorothy A. [*Trans. Ophthalmol. Soc. United Kingdom*, **71**, 361 (1951).]

Pathological and biochemical aspects are reviewed. There appears to be a disordered functioning of the adrenal and pituitary glands, leading to retention of NaCl and water. Sufficient amounts of urea given over a long period will lessen the frequency and severity of attacks. W. C. Tobie (Chem. Abstr.)

Urinary Excretion of 17-ketosteroids in Schizophrenics. Lingjaerde, O., and Støa, K. [*Tidsk. Norske Laegeforen.*, **69**, 181 (1949.]

Data on the excretion of 17-ketosteroids (I) by psychotic patients, mostly with schizophrenia (II), are tabulated and discussed. In most cases the values for (I) were normal but were sometimes very low, especially in the active and stuporous forms of (II).
W. C. Tobie (Chem. Abstr.)

Multiple Sclerosis. Rademaker, G. [*Vorderingen Geneeskunst*, 1945-48, 343 (1949).]

A review and discussion, including the role of Cu, Co, I, F, and Mn deficiencies in diminishing resistance. W. C. Tobie (Chem. Abstr.)

A Tetanic Syndrome without Changes in Chemical Composition of the Blood in a Case of Juvenile Dementia Paralytica (Lissauer). Fahr's Idiopathic Perivascular Calcification. van Bogaert, L. [*Monatsschr. Psychiat. Neurol.*, **118**, 30 (1949).]

Mainly pathological with a discussion of the physical and chemical origin of perivascular calcifications in the brain. W. C. Tobie (Chem. Abstr.)

Levels of Blood Oxygenation of Blood in Schizophrenic Patients. Tsikhanshkaya, Z. S. [*Nevropathol. i Psikhiat.*, **17**, *No.* 6, 33 (1948).]

Toluidine blue (I) acts as an oxidation-reduction indicator in staining hemoglobin (II) giving green-yellow at +100 mv., blue at −10 mv., to pinkish-violet at −70 mv., depending upon the degree of oxidation of (II). Of 60 normal subjects, the blood of 48 stained green (+50 mv.), that of the other 12 was in the positive range, blue-green to yellow-green. Over 400 determinations were made on the blood of 30 schizophrenic patients. The blood usually stained blue-green (−25 mv.). In catatonia, the potentials were very low, showing low oxygenation of (II). In 4 of 5 cases of chorea, oxidation levels were very high. The effects of intravenous honey injections on the hematology of schizophrenics are described. In 10 of 17 cases, the oxidation potentials of (II) were restored (temporarily?) to normal values, with clinical improvement. W. C. Tobie (Chem. Abstr.)

The Clinical Significance of Electrophoretic Studies of Cerebrospinal Fluid and Serum in Acute Anterior Poliomyelitis. Olderhausen, H. F. v., et al. [*Deut. Z. Nervenheilk.*, **170**, 254 (1953).]

In the early stages of the disease α_1- α_2- and β- globulins were increased and albumin was decreased in serum, as measured by paper electrophoresis. In cerebrospinal fluid an increase in albumin and γ-globulin and a decrease in other fractions appeared after 2-4 weeks. Warren M. Sperry (Chem. Abstr.)

Metabolic Disturbances and the Central Nervous System. Peters, Gerd. [*Deut. Z. Nervenheilk.*, **169**, 446 (1953).] Warren M. Sperry (Chem. Abstr.)

Biochemical Studies on the Action of Nerves. VI. Cholinesterase in the Cerebrospinal Fluid. Okinaka, Shigeo, et al. [*Igaku to Seibutsugaku* (*Med. and Biol.*), **25**, 10 (1952).]

Results are given of determinations of cholinesterase (I) of some 140 cerebrospinal fluids from normal and diseased humans. The enzyme activity was given as cu.mm. CO_2 evolved in 30 minutes at 37·5° per ml. cerebrospinal fluid. (I) Values varied from 4·8 (in Heine-Medin disease) to 182·0 (in spinal tumor) and were as follows: normal humans (10 cases), $16·9 \pm 1·41$; tuberculous meningitis (16 cases), $38·8 \pm 12·4$; poliomyelitis anterior (18 cases), of which 4 showed normal values and 14 decreased activities ($11·1 + 4·17$); brain tumors (12 cases), of which 4 showed decreased activities and the others more or less increased activities (the highest value, 151·0, was observed in Hippel-Lindau disease). The significance of these results in clinical diagnosis was discussed. M. Nakamura (Chem. Abstr.)

Phosphatase and Nucleic Acids in Centers of Cerebral Hemorrhage. Gherarducci, D. [*Sistema nervoso*, **4**, 518 (1952).]

In 6 rabbits injected with paraffin oil a constant increase of phosphatase, a decrease of the ribonucleic acid, and no change of the thymonucleic acid were observed in the centers of cerebral hemorrhage. C. Scandura (Chem. Abstr.)

17-Ketosteroid Changes in Cerebral Apoplexy. Gherarducci, D. [*Sistema nervoso*, **4**, 520 (1952).]

The 24-hour urinary 17-ketosteroid excretion was normal or greater than normal (maximum 25 mg.) in 19 patients. C. Scandura (Chem. Abstr.)

Acetylcholine in the Cerebrospinal Fluid (*CSF*) *of Neuropsychic Patients. Poloni, A., and Maffezzoni, G.* [*Cervello*, **28**, 15 (1952).]

The following observations were made: (1) The absence of acetylcholine (1) in the CSF of patients with progressive paralysis had no connection with luetic antibodies, albumin, globulins, and cell elements; (2) (1) was higher in epileptic patients before the convulsion and decreased thereafter; (3) the CSF of schizophrenic patients showed no (1); (4) in paraphrenic patients the presence of (1) was observed; (5) the brain fluid showed more (1) than the spinal fluid in nonschizophrenic patients; (6) acetylcholine administration to schizophrenic and nonschizophrenic patients caused an increase of (1); (7) electroshock (e.s.) raised (1) in nonschizophrenic patients, and lowered it in the schizophrenic ones; (8) paraphrenic patients showed a decrease of (1) after electroshock; (9) (1) increased in schizophrenic patients during insulin therapy; (10) in recovered schizophrenic patients (1) appeared; (11) in recovered schizophrenic patients e.s. lowered (1), and this response was not influenced by a previous treatment with pregnenolone. G. Scandura (Chem. Abstr.)

Lactic Acid of Blood and Pyruvic Acid of Blood in Schizophrenia. Torre, L. Dalla, et al. [*Lavoro neuropsichiat.*, **10**, 3 (1952).]

In 20 patients the average lactic and pyruvic acid contents of blood were 16·95 and 1·54 mg. per cent. respectively. C. Scandura (Chem. Abstr.)

Fluorescence Quantitative Spectrophotometry of Cerebrospinal Fluid (*CSF*) *in Schizophrenia. Salvi, P., and Zara, E.* [*Acta Neurol.*, **7**, 49 (1952).]

The fluorescence spectrum (ultraviolet excitation) of the CSF of schizophrenic patients was nearly normal but less intense, especially in the violet band where the intensity was nearly 70 per cent. that of normal CSF. This is interpreted as a low concentration of pterin compounds. C. Scandura (Chem. Abstr.)

The Roles of Emotional Stress and Diet in the Etiology of Diabetes Mellitus. Simon, Norman M., and Mirsky, Stanley. [*Quart. Bull. Northwestern Univ. Med. School*, **27,** 126 (1953).]

Anxiety produced by electric shock, in combination with a high-fat diet, significantly increased the blood glucose of rats without producing clinical diabetes. The role of emotional stress in the etiology of diabetes mellitus in man is probably that of a triggering mechanism that may set off the chain of pathological reactions in individuals predisposed by dietary or other factors. MARION HORN PESKIN (Chem. Abstr.)

Fever and Brain Metabolism. Tasaka, Sadataka and Ishihara, Makoto. [*Igaku to Seibutsugaku* (*Med. and Biol.*), **26,** 266 (1953).]

During fever, the production of pyruvic and lactic acids were increased in the brain tissue. M. NAKAMURA (Chem. Abstr.)

The Effects of Carbon Dioxide Inhalation upon the Cerebral Blood Flow and Cerebral Oxygen Consumption in Vascular Disease. Novack, Paul, et al. [*J. Clin. Invest.*, **32,** 696 (1953).]

The effects of inhalation of 5 per cent. CO_2 upon the cerebral circulation of individuals with varying degrees of vascular disease were studied. The normal response to an elevation of arterial pCO_2 is a slight increase in the mean arterial blood pressure and a drop in cerebrovascular resistance with a consequent increase in cerebral blood flow. A group of normotensive arteriosclerotic individuals failed to show significant decrease of the cerebrovascular resistance, although the cerebral blood flow increased slightly. A small group of uncomplicated essential hypertension cases responded normally to CO_2 inhalation. A group of hypertensive arteriosclerotic patients responded normally to CO_2 but the residual cerebrovascular resistance after CO_2 vasodilation was still markedly above normal. The response to CO_2 inhalation seems to provide a convenient means for dissociating and establishing the components of an increased cerebrovascular resistance attributable to functional vasoconstriction and arteriosclerotic narrowing of the lumen of the vessels. JOHN T. MYERS (Chem. Abstr.)

Cerebral Circulation and Metabolism in Pulmonary Emphysema and Fibrosis with Observations on the Effects of Mild Exercise. Scheinberg, P., et al. [*J. Clin. Invest.*, **32,** 720 (1953).]

Cerebral blood flow, O consumption, and vascular resistance were measured in 22 patients with chronic pulmonary disease of moderate functional severity, and compared with normals of the same age. The effect of mild exercise was studied in 12 of the patients. There was no significant difference in cerebral blood flow measured by the intermittent sampling technique as compared to continuous sampling. Mean values for cerebral blood flow, cerebral arteriovenous O difference, cerebral O consumption, and cerebral vascular resistance did not differ in patients and normals. The correlation between cerebral blood flow and arterial pCO_2 was good, whereas no correlation was found between cerebral blood flow and arterial pO_2 or percentage arterial O saturation. The effect of exercise was variable. A reduction in arterial pH during exercise did not influence cerebral blood flow. JOHN T. MYERS (Chem. Abstr.)

Lipide dystrophic Changes in the Central Nervous System in Dogs. Hagen, L. O. [*Acta Pathol. Microbiol. Scand.*, **33,** 22 (1953).]

The histological and clinical picture is described in 2 dogs with lipide dystrophy of the central nervous system. The changes consisted of deposition of complex lipides in the neuron cells in the brain and retina, producing among other things, blindness. The lipides, according to their solubility and biochemical reactions, seemed to be largely phosphatides. There was a pronounced gliosis in the cerebellum, loss of cells in the granular cells, and loss of Purkinje cells. The changes closely resemble those of amaurotic familial idiocy in man.
JOHN T. MYERS (Chem. Abstr.)

Apparent Significance of Melanin in the Substantia Nigra. Friede, Reinhard. [*Naunyn-Schmiedebergs Arch. exptl. Pathol. u. Pharmakol.*, **218,** 286 (1953).]

The ganglion cells of the substantia nigra are able to form melanin from adrenaline. The pigment disappears in parkinsonism. Parkinsonism responds to sympathomimetic and parasympathicolytic drugs. Melanin is related to a process of metabolism of tyrosine derivatives.
A. E. MEYER (Chem. Abstr.)

Microchemical Studies of the Nervous System. X. Cerebrosides of Nerve during its Degeneration. May, Raoul Michel and Thillard, Marie Jeanne. [*Bull. soc. chim. biol.*, **35,** 307 (1953).]

The cerebrosides of the sciatic nerve (dog) increased 60 per cent. or more during the first 3 days after section, then decreased to about half the presection value in the next 9 days. There was little change thereafter. L. E. GILSON (Chem. Abstr.)

Changes of Lipide Phosphorus in Blood Induced by Electrical Stimulation of the Hypothalamus of Rabbits. Inoue, Kazumasa. [*Osaka Daigaku Igaku Zasshi*, **5,** 457 (1953).]

The concentration of lipide P in blood (1) was 2·76 to 13·74 mg. per cent. in 35 normal fasted rabbits. After the stimulation of the ventromedial hypothalamic nucleus, the concentration of (1) decreased in 8 cases, increased in 5 cases and remained unchanged in 2 cases out of all 15 animals. These changes were observed within 1 hour after the stimulation. By the stimulation of the lateral hypothalamic nucleus, the concentration of (1) increased in 11 cases

out of 15, remained unchanged in 3, and decreased in one case. These increases were produced within 2 hours after the stimulation and the maximum increment was 1·38 to 4·08 mg. per cent.
ITIRO TYUMA (Chem. Abstr.)

Brain Metabolism during Acclimatization to High Altitude. Albaum, Harry G., and Chinn, Herman L. [*Am. J. Physiol.*, **174**, 141 (1953).]

Acclimatization of rats to lowered barometric pressure equivalent to 11,000, 18,000, and 22,000 ft. did not alter significantly the levels of the brain constituents determined. In rats breathing N for 3 minutes, the brain adenosine triphosphate (ATP), adenosine diphosphate, phosphocreatine, organic P, and glycogen decreased while the inorganic P, lactic acid, and adenylic acid increased. No change in the activity of brain cytochrome oxidase was apparent after acclimatization. The rate of P^{32} incorporation into brain ATP was unaltered after acclimatization.
E. D. WALTER (Chem. Abstr.)

Mitochondrial Preparation from Mammalian Brain. Brody, T. M., and Bain, J. A. [*J. Biol. Chem.*, **195**, 685 (1952).]

Differential centrifugation in 0·25 M sucrose of homogenates of rat or rabbit brain yields a fraction (1) having histological, chemical and metabolic properties similar to those of liver mitochondria. (1) Oxidizes at high rates the majority of the Krebs citric acid cycle intermediates and glutamate. With the addition of an adenine nucleotide (either adenosine triphosphate, adenosine diphosphate, or adenylic acid) and of yeast hexokinase associated phosphate uptake, with P:O ratios of 2·5 to 3·0, is demonstrated. (1) Does not oxidize at appreciable rates alanine, aspartate, or octanoate, nor does it exhibit any glycolytic activity.
J. P. DANEHY (Chem. Abstr.)

Attempt at a Theory of Cellular Excitability. Nervous Flux; Automatisms. 1. Gibert, Rene. [*J. chim. phys.*, **49**, 448 (1952).]

A system of 4 schematic chemical equations is set up in such a way that their kinetic behavior would show precise analogy to certain aspects of the behavior of excitable matter. In particular, it obeys the "all-or-nothing" law necessary to account for the discharge of impulses by nerve cells. Only broad specifications can be given for the nature of the chemical entities postulated. The relations among reaction velocities and among concentrations necessary to cause the system to return to its initial state, and thus to account for the phenomena associated with automatisms, are discussed.
T. H. DUNKELBERGER (Chem. Abstr.)

A Comparative Study of the Lipide Composition of the Brain in Various Vertebrate Classes. Bieth, R., and Mandel, P. [*Experientia*, **9**, 185 (1953).]

Analysis of total lipides, phosphatidic fatty acids, and sphingomyelin of the brains of carp, turtle, duck, domestic fowl, rat, guinea pig, cat, dog, and man shows an increase in the ratio of these to the species characteristic quantities of deoxyribonucleic acid of the diploid chromosome group; this increase is regarded as parallel to phylogenetic position.
D. S. FARNER (Chem. Abstr.)

Amyotrophic Lateral Sclerosis. Spies, T. D., and Stone, R. E. [*Southern Med. J.*, **42**, 410 (1949); *Excerpta Med., Sect. VIII*, **2**, 916 (1949).]

In 5 cases (without anemia), injections of vitamin B_{12} decreased muscle cramps and fibrillation and briefly delayed the progress of the disease, but without improvement in the abnormal physical signs.
W. C. TOBIE (Chem. Abstr.)

Quantitative Determination of Ribonucleic Acid from Individual Nerve Cells. Edstrom, Jan Erik. [*Biochem. et Biophys. Acta*, **11**, 300 (1953).]

A method is described for the determination of ribonucleic acid (RNA) in individual nerve cells; this method involves dissection of fixed cells into individual cells, determination of the cell volume, extermination of the cell with buffered ribonuclease solution and microspectrophotometric est of the (RNA) content of the extract. The accuracy of the method applied to fixed nerve cells of size $20\times10^3-60\times10^3$ μ^3 is at least ±4 per cent. The mean (RNA) concentration of 12 individual motor anterior horn cells was 0·67 −0·10 per cent., values for individual cells varying from 0·18 to 1·29 per cent.
MORTON PADER (Chem. Abstr.)

Acetylcholine in the Brain in Various Functional Stages. Herken, Hans and Diether, Neubert. [*Naunyn-Schmiedebergs Arch. exptl. Pathol. Pharmakol.*, **219**, 223 (1953).]

Killing rats with liquid air offers no advantage in the determination of acetylcholine (I) as compared with other methods. No change in the (I) was found in electroshock, metrazole, or schilliroside convulsions. Narcosis causes a marked increase in (I). The same effect of intravenous injection of eserine is based on a different mechanism. Metrazole can normalize the (I) content in narcosis. Prostigmine causes a slight increase. p-Nitrophenyl diethyl phosphate (II) produces an increase at the same rate as eserine. The symptoms of poisoning by (II) in mice are prevented by pretreatment with some hexachlorohexanes.
A. E. MEYER (Chem. Abstr.)

Structural and Cytochemical Modifications in the Anterior Radicular Cells of the Spinal Medulla of Fatigued Animals. Mangione, Francesco. [*Rass. Med.*, **30,** 53 (1953).]

Radicular spinal cells of the cervical and lumbar-sacral segments of fatigued rats showed a progressive decrease in cytoplasmic ribonucleic acid. The amount of decrease depended on the extent of fatigue. The ribonucleic acid was restored during the resting phase. In extreme fatigue, the nucleolus maintained the normal amount of ribonucleic acid while its deoxyribonucleic acid diminished. Thus the fulcral role in cellular protein synthesis played by the nucleolus was put in evidence. The experimental observations were carried out by means of known staining reactions of the chromophilic substance of the cells. P. T. Izzo (Chem. Abstr.)

Ocular Phenomena of Postencephalitic Parkinsonism. Crow, J. [*Glasgow Med. J.*, **30,** 29 (1949); *Excerpta Med., Sect. VIII*, **2,** 911 (1949).]

Pathological features of 80 cases are described. Inhalation of iso-Amnitrite failed to produce oculogyric crises, hence these crises probably result from vestibular action rather than emotional stimulation. W. C. Tobie (Chem. Abstr.)

Autolysis in Normal and Pathological Cerebrospinal Fluids. Kovacs, Ernest. [*Can. J. Med. Sci.*, **31,** 358 (1953).]

The acid-solution P concentrated of 850 specimens of cerebrospinal fluid (CSF) was determined before and after incubation under standardized conditions. P changes resulted from interaction of enzymes and P-containing organic material in the CSF. Normal CSF, and a large number of poliomyelitis specimens, exhibited no P changes after incubation. In the CSF of acute bacterial meningitides a great increase of P usually occurred and a great increase was found in active neurosyphilis. The CSF of idiopathic epileptics and of patients with post-traumatic syndrome showed high P release. The CSF in cases of brain tumor manifested moderate changes. A. E. Terri (Chem. Abstr.)

Antidiuretic Action of Cerebrospinal Fluid. Butturini, U., and Marinoni, U. [*Riforma med.* **63,** 193 (1949); *Excerpta Med., Sect. VIII*, **2,** 903 (1949).]

In human and bovine cerebrospinal fluid (I) the spinal fluid had more antidiuretic action (II) than the cerebral fluid, contrary to other reports. The (II) of (I) is probably identical with that of the posterior-pituitary gland. However, (I) also contains a diuretic substance and one influencing Cl metabolism. The action of (I) on urine flow probably results from 2 antagonistic hormones of pituitary origin. W. C. Tobie (Chem. Abstr.)

A Chemical Phase in the Transmission of Nervous Effects. Dale, Henry. [*Endeavour*, **12,** 117 (1953).]

For some 50 years, evidence has been accumulating which indicates that transmission across cell junctions occurs by chemical means, and that a principal agent involved is the ester acetylcholine. The history of the subject is surveyed. S. Tolansky (Chem. Abstr.)

The Nervous Impulse. Spadoline, I. [*Sistema nervoso*, **1,** 3 (1949); *Excerpta Med., Sect. VIII*, **2,** 891 (1949).]

A review and discussion, including a new theory of electrochemical transmission in synapses. W. C. Tobie (Chem. Abstr.)

The Cerebral Circulation and Metabolism in Arteriosclerotic and Hypertensive Cerebrovascular Disease, with Observations on the Effects of Inhalation of Different Concentrations of Oxygen. Heyman, Albert, et al. [*New Engl. J. Med.*, **249,** 223 (1953).]

The mean cerebral blood flow was somewhat less in older control subjects than in young healthy patients and was greatly reduced in patients with cerebrovascular accidents. The cerebral O consumption was reduced markedly by chronic cerebrovascular disease, but only slightly reduced by a single acute vascular accident, and was slightly less in the older than in the younger group of healthy persons. Cerebral blood flow in patients with cerebrovascular accidents was reduced by administration of 85-100 per cent. O, but little affected by administration of 50 per cent. O. The O uptake of the brain was unaffected by O administration at either level. Because of the vasoconstrictive effect of 100 per cent. O inhalation, use of this concentration in patients with cerebrovascular accidents should probably be avoided.

Marion Horn Peskin (Chem. Abstr.)

Poliomyelitis-like Cerebrospinal-fluid Findings in Cattle from Farms with Cases of Human Infantile Paralysis. Frauchiger, E., and Schmid, G. [*Schweiz. med. Wochschr.*, **79,** 316 (1949).]

Pathological changes, including increased cell count and protein content, as well as changes in sugar content, are described. W. C. Tobie (Chem. Abstr.)

Pathology of the Meninges in Relation to the Hematoencephalic Barrier. 1. Small Arachnoidal Plaques. Dina, M. A. [*Riv. sper. freniat. e med. legale alienazioni mentali*, **72,** 293 (1948).]

The plaques originate from protein thesaurismosis, and consist of a hyaline substance, osteoid. They are rarely calcified. W. C. Tobie (Chem. Abstr.)

A Case of Familial Recurrent Paralysis. Study of Potassium Metabolism. Malaguzzi-Valeri, C. [*Progr. med.* (*Naples*), **5,** 83 (1949); *Excerpta Med., Sect. VIII*, **2,** 924 (1949).]

Serum K was low (14-16 mg. per cent.) and at the beginning of an attack decreased to 6·07 mg. per cent. After injection of adrenal cortex extracts it dropped to 9 mg. per cent. and remained at this level for 2 hours without causing symptoms. This indicates that the muscle K is of main importance, not the blood K. After 5 g. of KCl orally, blood K increased to a maximum of 19·52 mg. per cent. after 2 hours, then decreased. The tissues appeared to be "thirsty" for K salts. Giving KCl after adrenocortical extract increased the blood K only slightly. The role of K in muscular contraction is discussed. Low K levels may be associated with insulin coma and with the asthenia accompanying infectious diseases. Paralysis from low K levels can be produced experimentally. W. C. Tobie (Chem. Abstr.)

Sarcoma Caudae Equinae with Hypothalamic and Bulbar Disturbances (*Syndrome of Simmonds*). *Brouwer, B., and Posthumus Meyjes, F. E.* [*Proc. Acad. Sci. Amsterdam*, **51,** 285 (1948); *Excerpta Med., Sect. VIII*, **2,** 921 (1949).]

Pathological features in a girl of 14 are described. There was diabetes insipidus, but disturbances of carbohydrate metabolism were not present, showing that in chronic lesions the paraventricular nuclei may be seriously damaged without producing glycosuria or hypoglycemia. W. C. Tobie (Chem. Abstr.)

Prognosis of Injuries of the Skull, Based on Examination of the Cerebrospinal Fluid. Guszich, A [*Orvosi Hetilap*, **90,** 216 (1949); *Excerpta Med., Sect. VIII*, **2,** 903 (1949).]

The cerebrospinal fluid (I) normally contains no NH_3 (II) but (II) appears in states of excitation (III). When (III) is localized in the brain stem, the amount of (II) is 0-120γ per cent.; when (III) reaches the cortex the (II) concentration is 450-500γ per cent. in infants and children and 1,500-3,000 in adults. Determination of (II) in (I) is helpful in the localization of nervous lesions and in prognosis. Average amounts of (II) (in γ per cent.) are: in concussion 112-1,420 (in fatal cases 1,500-1,900); in contusion 781-1,650; in 2 fatal cases of cerebral peduncle hemorrhage 97-112; in subdural hematoma 70-240; in indentation of the skull 790-1,250. In fractures of the base of the skull with unconsciousness, the amount did not exceed 1,390γ per cent.; in fatal cases 1,260-3,050. Amounts of (II) of 110-120γ per cent. may indicate lesions of the midbrain and brain stem and may be as serious as values above 1,800. With values above 2,000γ per cent. the prognosis is bad. W. C. Tobie (Chem. Abstr.)

Glycolysis in the Brain. Lenti, C. [*Boll. soc. ital. biol. sper.*, **28,** 1969 (1952).]

Brain homogenate does not produce more lactic acid from glucose in the presence of ferrous sulfate or of glutathione than from glucose alone. M. Elliott (Chem. Abstr.)

A General Method for the Preparation of Cerebrosides. Uzman, L. Lahut. [*Arch. Biochem. Biophys.*, **45,** 149 (1953).]

A new method applicable to spleen and brain tissue for the large-scale preparation of cerebrosides is described. It involves the extraction of total lipides from fresh tissue with a boiling $CHCl_3$-MeOH mixture and isolation of the cerebrosides by virtue of their property of accumulating at the interface when diluted Cl_3CCO_2H is added to the lipide extract. Cerebroside preparations thus obtained account for 65-75 per cent. of the total tissue cerebrosides. Infrared absorption spectra are presented for preparations from cattle brains and from 3 spleens from patients with Gaucher's disease. Felix Saunders (Chem. Abstr.)

The Concept of a Damping Effect and its Applications in Nervous Physiology. Monnier, A. M. [*Anales inst. farmacol. espan.* (*Madrid*), (**1**) 99, (1952).]

Discussion of a new characteristic nervous function based on the physical concept of "amortissement" (damping?) (I). It represents the stability of the nerve, its opposition to activation by external or spontaneous stimulation. It is measured by applying to the nerve 2 electrical stimuli separated by a variable interval. The first stimulus is adjusted to a subminimal value so that no response is evoked. The second stimulus is applied at varying intervals. The intensity of the second stimulus is adjusted each time to obtain a response. There is plotted the intensity of the second stimulus as a function of the interval separating it from the first stimulus. The effects of Ca^{++} deficiency, narcotics, chemical mediators, and CO_2 have been determined (I) is related to the membrane potential of the nerve and is suggested as an indirect measurement that can be performed *in situ* without necessitating electrodes in contact with the nerve. Superiority of (I) as a diagnostic technique over classical procedures is claimed because of the short duration of current flow and the minimal alteration of tissue during the test.
Herman I. Chinn (Chem. Abstr.)

Effect of Cortisone and Deoxycorticosterone (*DOC*) *on Carbohydrates in the Brain. Vaccari, F., and Rossanda, M.* [*Boll. soc. ital. biol. sper.*, **27,** 734 (1951).]

Normal and adrenalectomized rats were treated with cortisone and DOC, and the brain glycogen was determined. The average values were 1·640 mg./g. in controls, 1·206 in adrenalectomized rats, 1·379 in DOC-treated adrenalectomized rats, and 1·425 in cortisone-treated adrenalectomized rats. In normal rats, the total brain carbohydrate was 5·217 mg./g.

in controls, 5·250 in DOC-treated, and 5·256 in cortisone-treated rats; the corresponding figures for adrenalectomized rats were 4·760, 4·680, and 5·600 mg./g., respectively. Thus, cortisone exerts an effect on carbohydrate metabolism in the brain, but DOC does not.
B.A. (Chem. Abstr.)

Binding of Acetylcholine. Brodkin, E., and Elliott, K. A. C. [*Am. J. Physiol.*, **173,** 437 (1953).]
Maximum stability of the bound acetylcholine (ACh) in brain suspensions is found at about pH 7. The rate of breakdown increases rapidly above pH 8 and below pH 6. The rate of breakdown of bound ACh in brain is greatly accelerated, especially initially, by suspension in hypotonic medium and by high concentrations of K, Ca, or Mg ions. The presence of eserine seems to decrease the breakdown appreciably. The increased ACh content of normal brain slices incubated aerobically in the presence of glucose is accounted for mainly by bound ACh, which is extracted by acid but not by neutral medium. The bound ACh in brain suspensions is increased by the presence of ACh (30 γ/ml.) in the medium. Heart- and skeletal-muscle suspensions bind ACh slightly. No binding was detected with liver, kidney, or testis suspensions. Convulsant and narcotic drugs tested (other than ether) exerted no effects on liberation or binding of ACh by brain suspensions. E. D. Walter (Chem. Abstr.)

A New Chamber for Fixation of the Chemical Composition of the Brain of Rats in the State of Conditioned-reflex Block and Stimulation. Vladimirova, E. A. [*Doklady Akad. Nauk. S.S.S.R.*, **90,** 1191 (1953).]
The apparatus consists of a Plexiglass cylinder whose bottom is an electrode plate made of thin Cu strips. The top contains openings for ventilation. The cylinder is provided with side doors for passage of the animal to side chambers in response to stimuli. The bottom plate electrode can be excited to 15-20 v. for the nonconditioned stimulus. Photographs of the apparatus in use are shown and its use described in detail. For brain examination the apparatus is placed above a chamber with liquid O_2, into which the animal can be dropped instantly for fixation of the chemical composition of its brain. During the 1st 15 seconds of stimulation there is observed a rise in NH_3 in the cerebrum and a decrease during a longer stimulation (10 minutes). With conditioned-reflex block of the central nervous system for 120 seconds the content of NH_3 in the cerebrum dropped by 19 per cent. below normal. With stimulation of central nervous system there is an increase of 64 per cent. of NH_3 in rats that had been artificially waked from sleep; this was a 228 per cent. increase over the level found during normal sleep. G. M. Kosolapoff (Chem. Abstr.)

Effect of a Brain Fraction on Serum Cholesterol and the Serum-lipide Pattern. Gordon, Robert B., et al. [*J. Lab. Clin. Med.*, **41,** 583 (1953).]
Sheep brains were extracted with acetone and petroleum ether to yield a 0·312 per cent. cholesterol residue. This was fed to cockerels on high- and low-cholesterol diets and total cholesterol, total lipide, phospholipide, and ultra-centrifuge pattern determined after 14 days. On the low-cholesterol diet the controls lowered the serum cholesterol from 124 to 119 mg. per cent. while those fed the brain extract lowered from 124 to 104 mg. per cent. over the 14-day period. The final total lipide and phospholipide averaged 385 and 163 mg. per cent. in the controls compared to 382 and 143 mg. per cent. in those fed the extract. On the high-cholesterol diet the total cholesterol changed from 150 to 698 mg. per cent. in controls and from 139 to 306 mg. per cent. in those fed the extract. The total lipide was 1,444 mg. per cent. in the controls and 736 mg. per cent. in the extract-fed chickens. The phospholipide was 292 in the controls and 164 mg. per cent. in the extract-fed. Ultracentrifuge patterns showed reduction in the large peak in the Sf 20-70 range to half the control value. The authors feel that brain extract promotes the conversion of cholesterol to unabsorbable coprosterol in the bowel; this removes cholesterol from the body. Frank Iber (Chem. Abstr.)

The Action of Nervous Depressants on the Antidiuretic and Chloruretic Effects of Nicotine. Supek, Z., and Eisen, V. [*Arch. intern, pharmacodynamie*, **93,** 75 (1953).]
In hydrated rats, nicotine base (1·7 mg./kg.) produced an antidiuretic and pronounced chloruretic effect. Tetraethylammonium, diparcol, parpanit, pentamethonium, procaine, and atropine did not affect the excretion of water or Cl ions, either alone or after nicotine. Phenobarbital (130 mg./kg.) inhibited the antidiuretic effect of nicotine, and urethan increased it. The chloride excretion was increased by phenobarbital and not affected by urethan.
M. L. C. Bernheim (Chem. Abstr.)

Blood-iron Curves in Cases of Amentia and Schizophrenia. Ferroni, A., and Lipani, G. [*Acta Neurol. (Naples)*, **3,** 568 (1948).]
Intravenous injections of ferrocalcium or ferronascine (containing 7 mg. Fe) were made in 4 imbeciles and 24 schizophrenics. The former had a fairly normal serum-Fe response. Chronic schizophrenics showed retarded absorption of Fe. In acute (particularly hebephrenic) schizophrenia the serum-Fe was below normal both before and after the injections. In acute catatonia the differences from the normal were less marked. The paranoid cases showed deviations which were difficult to interpret. W. C. Tobie (Chem. Abstr.)

Psychophysical Correlations. VI. Experimental Investigation of the Problem of Schizophrenia. Mescaline Toxicosis and Liver Function. Georgi, F., et al. [*Schweiz. med. Wochschr.*, **79,** 121 (1949).]

In normal subjects, administering mescaline decreases the amount of hippuric acid excreted after giving Na benzoate and glycine. Persons with liver disease have an increased sensitivity to this test. Toxins believed to provoke schizophrenia may act in part upon the liver. W. C. Tobie (Chem. Abstr.)

Pathogenesis of Hepatocerebral Diseases. II. Histochemical Demonstration of Copper in the Liver. Okinaka, Shigeo, et al. [*Igaku to Seibutsugaku* (*Med. and Biol.*), **25,** 133 (1952).]

Cu reaction-positive granules were found histochemically in the livers of patients with Wilson's disease and with cirrhosis of the liver. The amount and the distribution of these granules differed in these 2 conditions. Pathological observations were discussed.

III. The Copper Metabolism in Wilson's Disease. Okinaka, Shigeo, et al. [*Ibid.* 209-12.]

The Cu concentrations of the livers of 2 patients with Wilson's diseases were: 34·78 (histochemically positive) and 13·1 mg. per cent. (negative). In control tests, the Cu contents were: subacute yellow atrophy, 14·29; cirrhosis of the liver, 14·0; in 15 other cases, below 8·3 mg. per cent. (the 1st 2 cases were histochemically positive). The Cu content of serum in Wilson's disease was 0·200 mg. per cent. and was not different from the normal values. However, the urinary excretion was (average) 0·764 mg./day and was far higher than the normal values. The amino acid content of the serum (total amino N) was 3·1 mg. per cent. and the maximum urinary excretion 150 mg./day. The urinary excretion of Cu in Wilson's disease increased at 1 and 2 days after the administration of 2, 3-dimercaptopropanol.

IV. The Relation Between the Cholinesterase of Basal Ganglia and Liver Diseases. Okinaka, Shigeo, et al. [*Ibid.*, 281-3.]

Results of determinations of cholinesterase activities are given for basal ganglia of 14 patients with liver diseases and of 14 patients with other diseases. No decrease in the enzymic activity was observed in liver diseases. M. Nakamura (Chem. Abstr.)

The Eye and the Diencephalon. XI. The behavior of "Light Sense" in the Tonus Changes of the Neurovegetative System. Tiberi, Gian Franco. [*Riv. oto-neurol-oftalmol.*, **25,** 285 (1950); *Am. J. Ophthalmol.*, **34,** 473 (1951).]

The light sense was studied in respect to changes in the tone of the neurovegetative system produced by sympathicotopic and parasympathicotopic compounds such as pilocarpine and atropine. The drugs apparently have a central (diencephalic) action and the light sense possibly responds differently to drugs affecting the vagosympathetic equilibrium as contrasted with those that act peripherally. W. C. Tobie (Chem. Abstr.)

Modern Views on Synapses in Relation to Neuropathology. Grashchenkov, N. I. [*Nevropatol. i Psikhiat.*, **17,** *No.* 4, 17-26 (1948).]

The pharmacological effects of neostigmine (1) in neuropathological conditions are discussed and reviewed, with reference to conditions of asynapsia, hyposynapsia, and hypersynapsia. The pharmacological effectiveness of (1) in tick-borne and mosquito-borne encephalitis indicates that a synaptic dysfunction is involved. In some brain injuries, α and β waves disappear from the electroencephalogram, followed by the appearance of new waves of great amplitude and frequency a few weeks later. If 1 ml. of 0·01 per cent. (1) is injected subcutaneously, normal waves reappear. W. C. Tobie (Chem. Abstr.)

Diencephalo-hypophyseal Diseases. Heller, E. F. [*Ärztl. Wochschr.*, **4,** 83 (1949).]

A girl with growth disturbances was observed for 12 years. During and after treatment with thyroid and later with anterior pituitary preparations, many diencephalo-hypophyseal symptoms (including abnormal blood Ca, albumin, and glucose levels) were seen, as well as absent or abnormal response to pilocarpine and adrenaline. Other pathological features are considered. W. C. Tobie (Chem. Abstr.)

Fluid and Electrolyte Exchange in the Brain in Experimental Convulsions. Adams, John E., et al. [*Trans. Am. Neurol. Assoc.*, **77,** 34 (1952).]

Tracer experiments with Na^{24} and P^{32} administered intraperitoneally to the golden hamster showed that convulsions produced by intraperitoneal injection of cocaine were followed by a shift of water and Na from the extracellular fluid into the cells of the brain. Marion Horn Peskin (Chem. Abstr.)

Electroencephalographic Effects of Intracarotid Injections of Diodrast. Foltz, E. L., et al. [*Trans. Am. Neurol. Assoc.*, **76,** 115 (1951).]

In normal monkeys anesthetized lightly with dial, intracarotid injection of diodrast (1) usually caused a seizure pattern on the electroencephalogram, but sometimes produced marked flattening and attenuation of activity on the side of injection. Cortical activation by (1) was inversely related to depth of anesthesia, was most marked in nonanesthetized subjects, and

was greater when the injected (1) solution was at 100° F. than when it was at room temperature, in studies on conscious and anesthetized monkeys and humans. In all cases with focal epileptogenic lesions of the cortex, (1) produced gross and startling activation of the epileptogenic focus, with clinical seizures in some cases. MARION HORN PESKIN (Chem. Abstr.)

Effect of Cortisone on Peripheral Nerve during Wallerian Degeneration. McColl, J. D., and Weston, J. K. [*Rev. can. biol.*, **12**, 68 (1953).]

The daily administration of 7·5 mg./kg. of cortisone acetate to cats for 16 days following sciatic nerve section had no effect on the edema which normally follows such section. The tensile strength of the 16-day degenerated nerves in the cortisone-treated group was statistically less than that of the nerves in the treated and non-treated (control) groups. Cortisone administration resulted in less total cellularity in the 16-day degenerated nerves and hence appeared to inhibit the cellular reaction. Cortisone administered in overdose appeared to inhibit protein (collagen) anabolism in Wallerian degeneration. The decrease in the concentration of the lipides associated with the myelin sheath (cerebroside, sphingomyelin, and free cholesterol) 16 days following nerve section was not significantly altered by cortisone. There was no significant difference in the tensile strength of the intact nerves as compared to the 16-day degenerated nerves in the untreated animals. A. PAPINEAU-COUTURE (Chem. Abstr.)

Unsaturated Fatty Acids in Neurological Diseases. Rossini, R. [*Riv. neurol.*, **19**, 141 (1949); *Excerpta Med.*, **3**, 176 (1950).]

Low-temperature ether extracts were made of serums in 66 cases of neurological disease. A high I no. (>0·70) was strong presumptive evidence of a neoplasm of the central nervous system. W. C. TOBIE (Chem. Abstr.)

Histological and Topographic Changes and Vulnerability Relations in the Human Brain in Oxygen-deficiency Edema, and Plasma Infiltration. 1. Definitions of Problems, Histological Aspects. Scholz, W. [*Arch. Psychiat. Nervenkrankh.*, **181**, 621-64 (1949).]

Mainly pathological and histological. In edema, exudates rich in protein gradually cause anoxemia and secondary cell changes (which are described) from lack of oxygen.
W. C. TOBIE (Chem. Abstr.)

2. Pharmacology and Treatment

Acute Barbiturate Poisoning. Lous, P., et al. [*Ugeskrift Laeger*, **111**, 349 (1949).]

Some 375 patients were studied. In 5 of the most severely poisoned cases (3 died) there were periods of a few seconds to several minutes when no cortical activity was recorded in electroencephalograms. Oliguria and increased blood urea nearly always occurred. Lower nephron nephrosis was sometimes observed. Methods of therapy are discussed.
W. C. TOBIE (Chem. Abstr.)

Chronic Barbiturism. Francone, M. P. [*Rev. med. cienc. afines* (*Buenos Aires*), (**11**), 179 (1949).]

The pharmacological properties and chemical structure of barbiturates are discussed in reference to chronic intoxication. W. C. TOBIE (Chem. Abstr.)

Combined Effects of Analeptics on the Central Nervous System: Influence of Electric Current on Spasmodic Action and on Toxicity. Ostrelko, O. P. [*Farmakol. i Toksikol.*, **16**, *No.* 1, 28 (1953).]

The convulsive dose of metrazole:coramine, metrazole:strychnine, and coramine:strychnine blends in frogs shows synergism; the threshold dose is smaller than for either component alone. In rabbits these blends show antagonism as to size of convulsive dose but not as to mortality; LD_{50} was only slightly sensitive to blending of the components.
JULIAN F. SMITH (Chem. Abstr.)

Cholinergic Activity of the Brain Tissue as Influenced by Bulbocapnine, Mescaline, and N, N-diethyllysergamide. Poloni, A., and Maffezzoni, G. [*Sistema nervoso*, **4**, 578 (1952).]

In guinea pigs, the administration of the diethylamide of lysergic acid, bulbocapnine, and mescaline (0·02-4, 50–100, and 20–100 mg., respectively) caused, respectively, an increase, a decrease, and no change of the cholinergic activity of the cerebral cortex.
C. SCANDURA (Chem. Abstr.)

Isoniazid in Cerebrospinal Fluid (CSF), Blood, and Urine. Ricci, G. G., et al. [*Aggiorn. pediat.*, **3**, 193 (1952).]

The administration of 1·45 mg. isoniazid (1) per kg. body weight to some patients with tuberculous meningitis caused the highest blood concentration of the drug at the 2nd-3rd hour. Higher doses caused higher and more lasting levels. The passage of the drug to the CSF occurred in the 1st hour. The subarachnoid administration of (1) maintained the CSF content for 10 hours. Nearly 40 per cent. of the administered (1) was excreted through the urine in 24 hours. C. SCANDURA (Chem. Abstr.)

Adenosine 5-monophosphate in the Treatment of Multiple Sclerosis. Lowry, M. Lester, et al. [*Am. J. Med. Sci.*, **226,** 73 (1953).]

Adenosine 5-monophosphate (My-B-Den) (I) given for 6-10 months to 16 patients with severe multiple sclerosis, produced an 86 per cent. improvement in endurance and a 72 per cent amelioration of bladder disabilities, and reduced the abnormally high pyruvic acid (II)/lactic acid (III) ratio in the blood toward normal. Incoordination, visual disturbances, spasticity, sexual weakness, and paresthesia were not helped by (I) or by brief trials of Fe adenosine 3-monophosphate, oral KCl, or adrenocorticotropic hormone. Best clinical results, without toxic reactions, were produced by 100 mg. (I) in aqueous solution 3 times/week, rather than by 20 mg. in gelatin. Multiple sclerosis may be a disease involving carbohydrate metabolism with a block at the (II)-(III) level. While search is being made for a more effective remedy, (I) warrants further investigation in the treatment of this disease and possibly other neuromuscular disturbances. MARION HORN PESKIN (Chem. Abstr.)

The Medical Aspects of Electric Shock Therapy (Including a Study of 192 Patients). Niesen, Edmond H., jr. [*Am. J. Med. Sci.*, **226,** 143 (1953).]

Among the effects described are the effects on extracellular fluid balance. Water metabolism and eosinophil count resemble those which occur after the administration of the 11-oxysteroids, but remissions are not the result of increased secretion of these hormones.
MARION HORN PESKIN (Chem. Abstr.)

Activation of Muscle Spindles by Succinoylcholine and Decamethonium. The Effects of Curare. Granit, Ragnar, et al. [*Acta Physiol. Scand.*, **28,** 134 (1953).]

Succinoylcholine (Sch) has a strong transient blocking effect on neuromuscular transmission due to depolarization of the motor end-plate. The effect has been studied by intra-arterial injection on single muscle spindles in cats. Spindle excitation by Sch was favored by an increase in stretch but could be elicited in completely slack muscles by slightly increasing the dose of Sch. Even after full paralysis of alpha motor fibers as well as gamma fibers by d-tubocurarine, the transient increase of discharge rate could still be elicited by large doses of Sch, but ultimately it paralyzed the gamma end-plates. Decamethonium also increased the discharge rate of muscle spindles but the effect lasted at least an hour and the irregular bursts of discharge could be blocked by large doses of curare. It is suggested that Sch, apart from its action on the gamma fiber end-plates, affects the sensory spindle organs directly.
S. MORGULIS (Chem. Abstr.)

Influence of Dihydrogenated Ergot Alkaloids (Hydergin) on Hypoglycemic Convulsions and Death. Osswald, H., and Rossel, W. [*Naunyn-Schmiedebergs Arch. exptl. Pathol. u. Pharmakol.*, **218,** 295 (1953).]

Hydergin significantly delays the onset of convulsions and death in rats and mice treated with convulsive doses of insulin. Postmortal investigation of the capillaries in the central nervous system showed that the effect is not caused by an improvement of the circulation in the brain. Pendiomid is able to prevent or assuage the vascular spasm produced by insulin but it has no influence on the time of convulsions and death. A. E. MEYER (Chem. Abstr.)

Treatment of Infectious Diseases of the Nervous System by Massive Doses of Vitamin B_1 and the Peculiarity of Its Action on Pain Syndrome. Evzerova, E. K., and Shinyanskaya, Ts. Ya. [*Vrachebnoe Delo.*, **27,** 587 (1947).]

Clinical tests with 1·5–3·0 g. vitamin B_1 total doses (parenteral) showed good results in most cases of pain and sensory disturbances caused by infections of the spinal-cord rootlets and spinal nerves. Motor disturbances are not in this category, as the results in such cases were very variable. If the sympathin content of the blood is super-normal, vitamin B_1 does not have the pain-relieving activity. G. M. KOSOLAPOFF (Chem. Abstr.)

Caffeine (use) in Morning Headaches in Hypertensive disease. Dmitrenko, L. F. [*Vrachebnoe Delo.*, **27,** 545 (1947).]

The morning headaches associated with hypertension appear to be caused by restricted venous blood flow in the brain. Caffeine appears to improve this circulation and reduces, therefore, the blood pressure within the cranium. G. M. KOSOLAPOFF (Chem. Abstr.)

Anticonvulsive Effect of Carbonic Anhydrase. Keller, Herbert. [*Klin. Wochschr.*, **31,** 617 (1953).]

Cardiazole convulsions in mice were counteracted by carbonic anhydrase injection.
ERICH HEFTMANN (Chem. Abstr.)

Anticonvulsant Properties of Mysoline, a New Antiepileptic Drug. Goodman, L. S., et al. [*J. Pharmacol. Exptl. Therap.*, **108,** 428 (1953).]

The pharmacological properties of mysoline (I) are compared with those of phenobarbital. The change in chemical structure from phenobarbital to (I) (replacement of the O in the urea moiety by 2 H atoms) does not alter the spectrum of anticonvulsant activity, but results in a less potent anticonvulsant agent as measured by several different tests. When (I) is given to rats and mice, crystals of phenylethylmalondiamide appear in the urine.
L. E. GILSON (Chem. Abstr.)

A Comparison of the Pharmacological Actions of Phenothiazine Derivatives Used in the Treatment of Parkinsonism. Hutcheon, Duncan E. [*J. Pharmacol. Exptl. Therap.*, **108,** 340 (1953).]

Diparcol, phenergan, and parsidol show the following effects: local anesthesia when injected intradermally in guinea pigs; inhibition of acetylcholine-induced contractions of the isolated guinea pig ileum; inhibition of salivary secretion induced by infusion of carbachol in anesthetized dogs; and lengthening of the refractory period of isolated rabbit auricles as measured by the decrease in the maximal rate of stimulation. Diparcol was the most active in all tests. In cats under chloralose diparcol did not inhibit gastric acid secretion provoked by histamine. L. E. Gilson (Chem. Abstr.)

Cytochrome Enzymes in the Brain and Liver of the Chronically Morphinized Rat. Wang, R. I. H., and Bain, J. A. [*J. Pharmacol. Exptl. Therap.*, **108,** 349 (1953).]

Brains and livers from chronically morphinized rats showed a decrease in liver diphospho pyridine nucleotide (DPN) cytochrome c reductase during morphinization and withdrawal, and a slight increase of brain and liver cytochrome c oxidase levels during morphinization followed by a marked decrease during withdrawal. No changes were observed in the malic dehydrogenase activity of either tissue. Brain DPN-cytochrome c reductase activity was not affected by the morphinization experiments. L. E. Gilson (Chem. Abstr.)

Arterial Hypertension by Veratrum Derivatives Injected into the Nervous Centers. Cicardo, V. H. [*Arch. intern. pharmacodynamie*, **94,** 65 (1953).]

The injection of Veratrum viride alkaloids into the cisterna magna, cerebral ventricles, or spinal cord in dogs is followed by marked hypertension, from stimulation of the vasomotor centers. Dibenamine, hydergin, priscol, and dihydroergotamine partly antagonize the effect. M. L. C. Bernheim (Chem. Abstr.)

Barbiturates and Phosphatases. Manzini, Attilio and Zoboli, Paolo. [*Arch. intern. pharmacodynamie*, **94,** 75 (1953).]

The alkaline phosphatase activities of brain, liver and kidney were measured after 1-10 days treatment of the rat with 5-ethyl-5′-methylthiobutyl-2-thiobarbituric acid or 5-isopropyl-5′-bromoallyl-3-N-methylbarbituric acid. The activities of brain and liver phosphatase were increased, and that of the kidney decreased. M. L. C. Bernheim (Chem. Abstr.)

Anticonvulsant Properties of Unsaturated Carbinols. Swinyard, E. A., et al. [*Arch. intern. pharmacodynamie*, **94,** 81 (1953).]

$HC{\equiv}CC(CH_3)(OH)C_2H_5$ (I), $HC{\equiv}CC(CH_3)(OH)CH{=}CH_2$ (II) and $HC{\equiv}CC(C_2H_5)(OH)CH{=}CH_2$ (III) all modify the seizures produced in laboratory animals by electric shock or metrazole and also raise the threshold for the production of seizures. (III) Is most toxic, most potent and of shortest duration. (I) Acts for longer than (II), and in larger doses affects the convulsions of patients receiving electric shock therapy.

M. L. C. Bernheim (Chem. Abstr.)

The Hypothalamic-cortical System in Barbiturate Anesthesia. Gellhorn, E. [*Arch. intern. pharmacodynamie*, **93,** 434 (1953).]

Increasing the depth of barbiturate anesthesia in cats is accompanied by the gradual loss of cortical "background" potentials, and diminution in the frequency of hypothalamic potentials. This is similar to the effect of hypercapnia. In deep anesthesia, the cortico-hypothalamic system may be unreactive, while the reactivity of the sensory projection areas is retained. M. L. C. Bernheim (Chem. Abstr.)

Influence of Some Narcotics and Sedatives on Blood Coagulation. Macht, David I. [*Arch. intern. pharmacodynamie*, **93,** 325 (1953).]

The clotting time of whole blood in rabbits is not influenced by codeine, papaverine, dihydromorphinone, dihydrocodeinone, methadone, cocaine, ether, $CHCl_3$, EtOH, urethan, barbital, phenobarbital, seconal, or nembutal. Morphine, procaine, novocaine, ethyl morphine, diacetyl morphine, N-allyl morphine, and demerol all promote blood clotting, approximately in decreasing order of activity. M. L. C. Bernheim (Chem. Abstr.)

The Effect of the Antihistaminic Drugs on the Central Nervous System in Rats and Mice. Heinrich, Max A. [*Arch. intern. pharmacodynamie*, **92,** 444 (1953).]

Phenindamine, tripelennamine, and prophenpyridamine were least active, thonzylamine, methapyrilene, ambodryl, and toladryl were fairly active and phenergan, diphenhydramine, antazoline, and chlorprophenpyridamine were quite active in potentiating the effects of hexethal and other hypnotic and narcotic drugs in rats. Amobarbital is least affected, secobarbital, pentobarbital, butabarbital, thiopental, hexethal, hexobarbital, chloral hydrate, urethan, and tribromoethanol are intermediate, and paraldehyde is most potentiated by diphenhydramine. Tolerance develops to diphenhydramine HCl with daily doses; at first, 10 mg. is equivalent to 6-9 mg. intraperitoneal Na hexethal. Amphetamine antagonizes hexethal and hexethal-diphenhydramine narcoses in rats, but the effect of caffeine was not predictable. Diphenhydramine usually antagonizes the loss of running ability caused in mice

by ether or chloroform, and potentiates the curariform action of ether in fatigue. The antihistamines do not appreciably alter the food intake or the spontaneous activity of rats or hamsters. M. L. C. Bernheim (Chem. Abstr.)

Neuromuscular Paralysis of Controlled Intensity and Duration Obtained by Perfusion with Succinylcholine. Reuse, J. J. [*Arch. intern, pharmacodynamie*, **92**, 417 (1953).]

In dogs, continuous perfusion of succinylcholine in different concentrations establishes a definite paralysis for varying periods of time, and does not affect the recovery period once the perfusion is stopped. M. L. C. Bernheim (Chem. Abstr.)

Activity and Toxicity of Certain Antiepileptics, Standardized by Means of Experimental Electrical Epilepsy. Frommel, V. Ed., et al. [*Arch. intern. pharmacodynamie*, **92**, 368 (1953).]

The effects of phenobarbital, diphenylhydantoin, phenacetylurea (I), and phenylethylacetylurea (II) on the thresholds for the tonic phase and coma during electrical epileptic fits in guinea pigs were studied. Phenobarbital is effective for electrical and chemical fits, but has hypnotic and depressive actions. Its therapeutic index (min. lethal dose/activity) is 6·3 for strychnine fits, 16 for coramine, 5 for metrazole, and 1·9 for electric shock. Diphenylhydantoin acts especially on the tonic phase, and its index is 1 for chemical shock, but 1·9 for electric shock. (I) Is not depressant, but may cause pathological changes in the liver and blood. Its index is 4·5 for strychnine, 3·3 for coramine, 15 for metrazole, and 7·6 for electric shock. (II) Is very effective in all kinds of seizures. Its index is 10·3 for strychnine, 14 for coramine, >10 for metrazole, and 5·1 for electric shock. M. L. C. Bernheim (Chem. Abstr.)

The Pharmacology of 3-chloro-10-(3-dimethylaminopropyl) Phenothiazine-HCl. A Substance which Potentiates Anesthetics and Causes Hibernation. Courvoisier, Simone, et al. [*Arch. intern. pharmacodynamie*, **92**, 305 (1953).]

The LD_{50} of 3-chloro-10-(3)dimethylaminopropyl-phenothiazine-HCl(R.P. 4560) intravenously for mice, rats, and rabbits is comparable to that of promethazine, isothazine, and diethazine; it is more toxic by mouth. It has a mild parasympatholytic action, and inhibits the secretion of HCl. It has a general antiadrenaline effect, but does not reduce adrenaline hyperglycemia. It is a mild antispasmodic. Intravenous injection into dogs of 0·5-5 mg./kg. produces mild hypotension and has little action on the heart. In rats it prevents, to some extent, the edema following ovalbumin or dextran, and has no effect on kidney function even after repeated doses. In high concentrations it inhibits blood coagulation, and depresses respiration in rabbits. It has little antihistamine effect. It has a marked potentiating effect on general anesthetics, both hypnotic and analgesic, and narcosis can thus be obtained with much smaller doses of the analgesic. With a curarizing drug, gallamine triethiodide, it does not increase the toxicity but aids in the induction and duration of the curarization. It increases the local action of procaine, and has some local anesthetic action of itself. It potentiates the narcotic effects of EtOH, and suppresses the excitation, and shows anticonvulsive effects against coramine and nicotine, but not strychnine. It has a strong hypothermic effect, greater than that of pyramidon, and suppresses thermoregulation. It reduces the respiratory exchange in nerve cells. The emetic effect of apomorphine is completely antagonized by it. It is very active against hemorrhagic shock in dogs and traumatic shock in rats.
M. L. C. Bernheim (Chem. Abstr.)

Local Anesthetic Effects of Sodium Amytal. Schiller, Francis. [*Anesthesiology*, **14**, 321 (1953).]

Sodium 5-isoamyl ethylbarbiturate in 4 per cent. isotonic solution has good local anesthetic properties when injected intradermally in human subjects or applied to frog sciatic-nerve preparations. In rhesus monkeys it produces spinal anesthesia before producing sleep when injected subdurally. Sodium secobarbital produces more profound and partly irreversible local anesthesia. Sodium phenobarbital has only very slight or no anesthesia. Sodium phenobarbital has only very slight or no anesthetic effect in human skin wheals.
Karl F. Urbach (Chem. Abstr.)

Recent Advances in the Study of Psychotonic Amines. Sabrié, R. [*Rev. méd. franç.*, **29**, 89 (1948); *Excerpta Med., Sect. VIII*, **2**, 881 (1949).]

The pharmacol. properties of d-amphetamine sulfate (dexedrine, maxilton) are discussed. It has a spectacular action against barbiturate coma. Other applications are described.
W. C. Tobie (Chem. Abstr.)

The Effects of Curare and Prostigmine on the Central Nervous System. Berman, S. [*Connecticut State Med. J.*, **12**, 1111 (1948); *Abstr. World Med.*, **6**, 269 (1949).]

The effects of curare (I) and of neostigmine (singly or together) on the reflexes, spasticity, and clonus in 21 neurological cases are described. Animal experiments indicate that the maximum action of (I) is subcortical, probably involving the motor centers of the brain stem. Twenty-seven references. W. C. Tobie (Chem. Abstr.)

The Neuromuscular and Ganglionic Blocking Action in Man of Bis(trimethylammonium) Decane (Diiodide) and Bis(trimethylammonium) Pentane Diiodide. Grob, D., et al. [*Bull. Johns Hopkins Hosp.*, **84,** 279 (1949); *cf. C.A.*, **45,** 4837h.]

The first drug gives muscular relaxation, the second is a ganglionic blocking agent.

W. C. Tobie (Chem. Abstr.)

Comparative Depression of Several Short-acting Barbiturates and Spirobarbiturates. Lee, Woo Choo. [*Japan. J. Pharmacol.*, **2,** 123 (1953).]

Spiro (2′-ethyl-3′, 5′-dimethylcyclopentane) barbituric acid (I) and its thio analog (II) produced a satisfactory hypnotic and anesthetic effect in rats and rabbits. The duration of action of both was the same. (II) Had a shorter duration of action than thiopental and surital and (I) had a shorter duration of action than pentobarbital and secobarbital. The thiobarbituric acid derivatives were longer acting than their nonthio analogs in growing rats.

Richard F. Riley (Chem. Abstr.)

Cure of Chronic Alcoholism by Apomorphine. Feldmann, H. [*Sem. hôp. Paris*, **29,** 1481 (1953).]

Apomorphine has in addition to its emetic effect an influence on the diencephalic emotivity, affectivity, nutritive, and impulsion centers as demonstrated by experiments with cats.

Geo. Sag (Chem. Abstr.)

The Effect of Cortisone and Deoxycorticosterone on Metrazole Convulsions in Mice. Leonard, Charles A., et al. [*J. Am. Pharm. Assoc.*, **42,** 442 (1952).]

Pretreatment with cortisone and deoxycorticosterone does not significantly affect metrazole-induced convulsions in mice.

David B. Sabine (Chem. Abstr.)

Stimulants of the Chemoreceptors and Blood-brain Barrier. Winterstein, Hans and Gokhan, Nurnn. [*Naunyn-Schmiedebergs. Arch. exptl. Pathol. Pharmakol.*, **219,** 192 (1953).]

Chemoreceptor stimulants such as NH_4Cl (H ions), lobeline, and NaCN lose their stimulating action on the respiration after extirpation of the carotid sinus receptors because they do not pass the blood-spinal fluid barrier. They regain their action by introduction into the 4th ventricle.

A. E. Meyer (Chem. Abstr.)

Action of Alcohol, Acetone, Ether, and Chloroform on the Chemoreceptors of the Glomus Caroticum. Landgren, S., et al. [*Naunyn-Schmiedebergs Arch. exptl. Pathol. Pharmakol.*, **219,** 185 (1953).]

Injections of EtOH, Me_2CO, Et_2O, or $CHCl_3$ in Ringer solution into the carotid artery of cats cause an augmentation of the action potentials of the sinus nerves elicited by the chemoreceptors. Atropine, d-tubocurarine, hexamethonium, and NH_3 inhibit the potentials partially or completely. This suggests that the narcotics used increase the chemical impulses in the glomus by inhibition of the cholinesterases.

A. E. Meyer (Chem. Abstr.)

Effects of Injection into the Cerebral Ventricles of the Dog. Central Action of the Compound. Cathala, H. P., and Pocidalo, J. [*J. Compt rend. soc. biol.*, **146,** 1709 (1952); *cf. C.A.*, **47,** 765b.]

Injection of 2 mg./kg. into the cerebral ventricle produced profound narcosis lasting 1-2 hours, hypothermia, and complete absence of hypertensive response to stimulation of the vagus or occlusion of the primary carotid arteries.

L. E. Gilson (Chem. Abstr.)

Correlation of the Uptake of Dye by the Mouse Brain with the Action of Strychnine. Romanov, S. N. [*Doklady Akad. Nauk. S.S.S.R.*, **89,** 753 (1953).]

Generally the resistance of the animal to strychnine bears a reciprocal relation to the ability of its brain to take up neutral red. Stimulation (electric) of peripheral nerves enhances this uptake, which decline to a minimum in 1 hour, then rises to a sharp maximum at 2 hours (reaching control level), declines to a minimum at 3-4 hours (which is higher than the 1st minimum) and rises to another maximum near control level at 5 hours. The resistance to strychnine (0·002 mg. per g. of body weight) in respect to onset of convulsions and time of death, plotted against time after nerve stimulation as above gave a picture that is substantially a mirror image of the uptake of neutral red. The animals given strychnine during the 2nd min. of dye uptake survived.

G. M. Kosolapoff (Chem. Abstr.)

Analgesic Power and the Question of Acute Tolerance to Narcotics in Man. Beecher, Henry K., [*J. Pharmacol. Exptl. Therap.*, **108,** 158 (1953).]

Repeated injections, at intervals of several hours, were made in patients having surgical pain. No evidence was found of the development of acute tolerance to the analgesic action of morphine, *l*-α-acetylmethadol, heptazone, 6-methyldihydromorphine, and metopon, either in terms of loss of effectiveness or in shortening of the effective period.

L. E. Gilson (Chem. Abstr.)

Comparison of Maximal Seizures Evoked by Pentylenetetrazole (Metrazole) and Electroshock in Mice, and their Modification by Anticonvulsants. Goodman, L. S., et al. [*J. Pharmacol. Exptl. Therap.*, **108,** 168 (1953).]

The type of convulsions produced by each method is discussed and the modifying and protective effects of tridione, paradione, phenobarbital, mebaral, phenurone, dilantin,

mesantoin, and thiantoin are described. The first 5 drugs are more potent against metrazole than against electroshock, and the last 3 are more potent against electroshock.

L. E. Gilson (Chem. Abstr.)

Comparison of Anticonvulsant Glycerol Ethers. Ginzel, K. H. [*Naunyn-Schmiedebergs. Arch. exptl. Pathol. Pharmakol.*, **212,** 331 (1951).]

Myanesin, myocaine (1) and 2 homologs of (1) given orally or intraperitoneally protect mice against lethal doses of metrazole and strychnine. The average protective doses are within the subparalytic range. With (1) the difference between protective and paralyzing dose is largest. All substances have a hemolytic effect which is smallest with (1). The point of attack is central. Neuromuscular block occurs with sublethal doses only.

A. E. Meyer (Chem. Abstr.)

Injections with Pure Glutamic Acid. Kergl, Ernst. [*Med. Monatsschr.*, **7,** 1516 (1953).]

The favorable effects of glutamic acid on the nervous system were obtained more rapidly and more conspicuously. An injection contained 1·5 g. glutamic acid and 0·15 g. glycine in 10 cc. H_2O.

A. E. Meyer (Chem. Abstr.)

Warburg's Theory of Narcosis. Rumme., Walter. [*Naunyn-Schmiedebergs. Arch. exptl. Pathol. Pharmakol.*, **212,** 177 (1951).]

The O consumption of human erythrocytes with cysteine-HCl (I) as activator in phosphate buffer of pH 7·4 and the influence of ethylurethan (II) were determined. At concentrations of (II) which were capable of causing total inhibition of respiration, the addition of (I) restored normal O absorption. Since the concentration of (II) was about 100 times that of (I) a molecule competition seems to be out of the question. The possibility of changes in the dielectric medium is discussed.

A. E. Meyer (Chem. Abstr.)

Electroencephalic Analysis of the Mutual Influence of Narcotic and Analeptic Drugs. Driesen, Wilhelm, et al. [*Naunyn-Schmiedebergs. Arch. exptl. Pathol. Pharmakol.*, **212,** 243 (1951).]

The cortical potentials in the cat inhibited by barbiturates were restored by metrazole (1). Coramine also causes suppression of the potentials which is reversed by (1). (1) Has only a mild restorative effect in Et_2O anesthesia. Convulsive discharges appear early. Coramine has no influence on the encephalogram in anesthesia and convulsive doses do not cause spastic discharges. (1) Also causes early spastic discharges in chloralose anesthesia. Conclusion: (1) and barbiturates have their point of attack in the brain stem, chloralose and Et_2O act on the cortex.

A. E. Meyer (Chem. Abstr.)

Urinary Colloidal Proteins during Electroshock Therapy. Gomirato, G., and Beghelli, G. [*Boll. soc. ital. patol.*, **(1),** 218 (1950).]

In 15 patients with depressive syndromes the colloidal protein content of urine averaged 15·02 and 66·95 mg. per cent. respectively, before and after 9 electroshock applications.

C. Scandura (Chem. Abstr.)

Potassium Permanganate in the Treatment of Status Epilepticus. Repin, N. I. [*Nevropatol. i Psikhiat.*, **17,** *No.* 2, 67 (1948).]

Of 600 cases of epilepsy given extensive biochemical investigation, about 30 were cases of status epilepticus (1). Intravenous injections of 20 ml. of O 1 per cent. $KMnO_4$ invariably terminated attacks of (1), often in 5-10 minutes. Results are attributed to an increased supply of O absorbed on erythrocytes, leading to oxidation of products of incomplete metabolism. Adsorbed Mn ions may also catalyze oxidation processes. The water in the injection has a hemolytic effect causing dispersion of colloids of plasma and of formed elements in the blood.

W. C. Tobie (Chem. Abstr.)

Peculiar Cerebral Lesions Caused by Depot Insulin in Dogs. Tobel, Friedabert. [*Arch. Psychiat. Nervenkrankh.*, **180,** 569 (1948).]

Cerebral changes produced in dogs and man by overdosage of insulin are described. The vulnerability of depancreatized animals to depot insulin is attributed to a profound alteration of metabolism including disturbed phosphorylation of hexose in the brain.

W. C. Tobie (Chem. Abstr.)

Antagonism between Succinic Acid and Barbituric Drugs. (I) Experimental Research on the Time of Narcosis, Respiration, and Blood Circulation. Zoboli, P. [*Acta anesthesiol. (Padua)*, **2,** 443 (1951).]

In dogs treated with hypnotic or toxic Na pentothal doses, the administration of succinic acid was scarcely efficient against the cardiovascular and respiratory collapses caused by the intoxication, and also inefficient in breaking or considerably shortening the barbituric narcosis.

(II) Electrocardiographic Research. Zoboli, P., and Dal Co. C. [*Ibid.*, 449.]

No changes of the electrocardiogram, as influenced by Na pentothal, were observed after succinic acid administration, even at high doses.

C. Scandura (Chem. Abstr.)

Anticonvulsant and Growth-inhibitory Effects of Some Organophosphorus Compounds. Ramaswami, Dasu and Kirch, Ernst R. [*J. Am. Pharm. Assoc., Sci. Ed.*, **42**, 495 (1953).]

The anticonvulsant action on mice (measured in terms of protection against electroshock and metrazole) and the selective inhibitory effect on germination of oat and yellow charlock seeds were tested in a series of dialkyl anilidophosphates in comparison with phenylurethan. In the series, dipropyl and dibutyl anilidophosphates were the most potent and the latter the most toxic. The regularity of the specific biological activity in the series is apparently due to their structural pattern with the —PONH group as the nucleus.

DAVID B. SABINE (Chem. Abstr.)

Experimental Study of the Neurotoxicity of Isoniazid and Its Prevention. Cahn, J., et al. [*Thérapie*, **8**, 62 (1953).]

In albino rats of 120-150 g. the LD_{50} of isonicotinic hydrazide, administered by intramuscular, intravenous, intraperitoneal, or subcutaneous route was 400-450 mg./kg. Simultaneous administration of antihistaminics did not significantly affect the lethal dose, but amobarbital 20 and 40 mg./kg. increased it, respectively to 825 and 1050 mg./kg.

GEO. SAG (Chem. Abstr.)

Death Due to Withdrawal of Barbiturates. Fraser, H. F., et al. [*Ann. Internal Med.*, **38**, 1319 (1953).] JOHN T. MYERS (Chem. Abstr.)

Excitant Action of Acetylcholine and Other Substances on Cutaneous Sensory Pathways and its Prevention by Hexamethonium and D-tubocurarine. Gray, W. W., and Gray, J. A. B. [*J. Physiol.*, **119**, 118-28 (1953).]

Intraarterial (i.a.) injection of 0·2 ml. of 10^{-5} g./ml. acetylcholine (I) into the skin of chloralose-anesthetized (100 mg./kg.) cats produced an outburst of centripetal action potentials. Intravenous (i.v.) skin injections of decamethonium (150-500 γ/kg.) did not diminish the sensory excitant action of injected (I) or depolarize the motor end-plates; similar results were obtained for atropine (1-4 mg./kg.) in smooth muscle. Ciba 7337, a sympathetic nerveending blocking agent (i.v., 5 mg./kg.), prevented pilomotor response of cat's tail tuft of hair as well as the sensory discharge (II) on close i.a. injection of (I) or of adrenaline (III). Effects of i.a. injection of (I) could not be mimicked by i.a. injection of (III) (in concentrations up to 10^{-4} g./ml.). These data indicate that the (II) produced by (I) is due to direct action on the sensory pathway. Close i.a. injection of nicotine and α-lobeline (0·2 ml. of 10^{-4} g./ml.) also produced (II). Hexamethonium (IV) (i.v., 20 mg./kg.) and d-tubocurarine (V) (i.a., 0·2 ml. of 10^{-3} g./ml.) prevented initiation of (II) by close i.a. injection of (I), but failed to block the responses to injected 1·2 per cent. KCl or to touch; (IV) and (V) do not exert their effects by blocking conduction in sensory nerves, but act similarly, to (I), nicotine, and α-lobeline.

MORRIS ROCKSTEIN (Chem. Abstr.)

Blood Proteins under the Influence of Electroshock. Bornschein, H., and Auerswald, W. [*Wien. Z. Nervenheilk.*, **2**, 164 (1949).]

The serum proteins (I) and hemoglobin (II) were determined before and for 60 minutes after electroshock in physically fit but psychotic patients. In agreement with Delay (I) increased to a maximum 2-5 minutes after the start of shock, then declined below initial values. Individual differences in initial (I) were related to muscular activity. The theory that increased (I) is mainly due to muscular convulsion was confirmed by experiments on dogs with and without curare. In a patient whose poliomyelitic paralysis prevented clonic convulsions, (I) increased only very slightly. (II) Regularly showed an increase, then a rapid fall to normal levels within 7·5 minutes. Curare did not modify these changes in (II). All plasma-protein fractions were equally involved in the increases in (I), which were associated with increased viscocity, n, and total N. There were no direct connections between the changes in (I) and in (II), the latter probably being produced by a central diencephalic mechanism, not by muscular activity.

W. C. TOBIE (Chem. Abstr.)

Acute Severe Barbiturate Intoxication. Kirkegaard, A. [*Ugeskr. Laeger*, **111**, 356-60 (1949).]

The chemical properties and pharmacological effects of barbiturates are discussed, as well as the treatment of overdosage. W. C. TOBIE (Chem. Abstr.)

Hypertensive Encephalopathy and Cerebral Arteriosclerosis. Russek, H. I., and Zohmna, B. L. [*N.Y. State J. Med.*, **49**, 1411 (1949).]

Caudal anesthesia with metycaine reduced the arterial pressure (I) in 4 cases of cerebral arteriosclerosis for several hours. Although (I) was rendered almost normal, cerebral complications (such as convulsions and paralysis) were unaffected. Increased (I) represents a compensatory mechanism. The use of antispasmodics such as papaverine is more justifiable than attempts to decrease (I). W. C. TOBIE (Chem. Abstr.)

The Barbiturate Test in Normal Individuals and in Patients with Organic Disease of the Nervous System. Šercl, Mir. [*Neurol. a Psychiat. Československá*, **12**, 102 (1949).]

Healthy, neurologically normal subjects (I) 8 hours after taking 0·3-0·4 g. phenobarbital (II) usually show a bilateral syndrome of cerebellum (III) deficiency, with horizontal nystagmus

in all cases. In persons under 30 there is also a vertical nystagmus in most cases. Other signs (which are described) are sometimes present, but a unilateral syndrome originating from the (III) is never shown. Nevertheless, except for certain tracts, (II) has little action on the (III) but acts mainly upon cellular tracts in the mesencephalon (IV). Confirmatory evidence is the fact that in fatal poisoning, (II) is mainly concentrated in the (IV). In patients with posterior fossa lesions, neurological signs from the action of (II) on the (III) are more pronounced. With lesions in the (IV) the signs are strongly pronounced, and are of value in diagnosis. The effects of prolonged intake of (II) in modifying the signs are discussed. Many references.

W. C. Tobie (Chem. Abstr.)

Comparative Effects of Analeptics and Multivitamin Preparations on Reflex Activity of the Central Nervous System in Anemic Frogs. Kudrin, A. N. [*Farmakol, i Toksikol.*, **16**, *No.* 3, 24 (1953).]

Frogs were given 0·5 ml. 1 per cent. caffeine-NaOBz solution, 0·4-0·5 ml. 0·01 per cent. picrotoxin, 0·5 ml. 0·5 per cent. coramine, 0·2-0·5 ml. 0·01 per cent. strychnine, or 0·5-1 ml. of a multivitamin preparation 30-50 minutes before inducing anemia by aortal ligature. Picrotoxin and coramine fortified the central nervous system against anemic paralysis; the others did not. Caffeine and strychnine, in after-treatments, accelerated recovery from the anemia paralysis; the vitamins had no effect in either case. The analeptics, in descending order of efficacy against anemia paralysis, are: picrotoxin, coramine, caffeine, strychnine.

Julian F. Smith (Chem. Abstr.)

Effect of Metrazole Shock on Adrenal Glands. Pekkarinen, A., et al. [*Acta Endocrinol.*, **6**, 257 (1951).]

Metrazole (I) shock was administered to rabbits by injecting 45-60 mg. (I) in 10 per cent. solution into the ear vein every other day for 3 weeks. During treatment the weight of the adrenal glands decreased 26 per cent.; the adrenaline increased 25 per cent., ascorbic acid 38 per cent., and cholesterol 121 per cent. Liver glycogen increased 30 per cent., spleen cholesterol 20 per cent. The weight of the spleen was reduced 15 per cent.; body weight and other organs remained practically unchanged. K. Schoen (Chem. Abstr.)

The Effect of Ion Exchange Resin in Epilepsy. Sheppe, Wm. M., et al. [*Trans. Am. Neurol. Assoc.*, **77**, 17 (1952).]

The K and NH_4 form of a cross-linked polyacrylic (carboxylic) cation exchange resin (I), given in daily dosage of 45 mg. with a 1,000 mg. Na diet to patients with severe epilepsy, rendered the electroencephalogram normal in 10 days. During (I) administration, the patients showed marked reduction in urinary Na and K, no change in serum Na, a slight decline in serum K, no change in CO_2 combining power or chloride or urea content of the blood, and an increased urine volume. Marion Horn Peskin (Chem. Abstr.)

Effects of Adrenocorticotropic Hormone (ACTH) and Cortisone in Multiple Sclerosis. Glaser, Gilbert H., and Houston Merritt, H. [*Trans. Am. Neurol. Assoc.*, **76**, 130 (1951).]

Among 33 patients with multiple sclerosis treated with ACTH sometimes followed by cortisone, 36 per cent. showed general but transitory improvement, without curative changes. Decreases and increases in cerebrospinal fluid protein, including γ-globin, accompanied treatment in some cases. Generalized asthenia sometimes appearing during therapy was not associated with lowered serum K but was occasionally relieved by KCl.

Marion Horn Peskin (Chem. Abstr.)

Synthetic Anticonvulsants. 1. Pharmacological Properties of 3-(2′-methylphenoxy) Propane-1, 2-diol and 3-(2′methoxyphenoxy) Propane-1, 2-diol. Omiya, Teruo. [*Folia Pharmacol. Japon.*, **49**, *No.* 2, 112 (1953); *Breviaria*, 12).]

The muscle-relaxing and anticonvulsant activities against convulsions induced by strychnine, picrotoxin, and metrazole were comparatively studies with 3-(2′-methylphenoxy) propane-1, 2-diol (myanesin) (I) and 3-(2′-methoxyphenoxy) propane-1, 2-diol (hustosil) (II) in mice. The PD_{50} (50 per cent. paralyzing dose) and LD_{50} (both per 10 g.) were, respectively: (I) 0·98 mg., 4·85 mg.; (II) 2·54 mg., 11·7 mg. (I) Inhibited the convulsion induced by strychnine with twice its PD_{50}. (II) Had lesser action. To the convulsion by picrotoxin, both (I) and (II) had weaker actions, the latter being slightly stronger. (II) Inhibited the convulsion by metrazole, with small administration while (I) was much weaker, suggesting that the difference is qual. Both (I) and (II) were hardly anticonvulsant to caffeine and camphor; but previous administration of a minute convulsant dose of the latter notably augmented and made longer the paralyzing action of (I) but not of (II). Against convulsion by benadryl (I) had no action.

II. Pharmacological Properties of Phenyl Glucosides. [*Ibid.*, 119; *Breviaria*, 13.]

The PD_{50} and LD_{50} were: o-toyl-α- 3·12, 11·2: β- 2·4, 8·5; guaiacol-α- 10·1, 27·0; β-glucoside 16·6, 25·0 mg./10 g. mice. α-Glucosides were more active in muscle relaxing than β-glucosides and with less severe side effects. Effects of these glucosides were somewhat delayed. The degrees of relaxation did not always parallel the doses. The 2 above α-glucosides,

in large amount, inhibited the convulsion by metrazole, but β-glucosides did not. All the glucosides above did not have anticonvulsant action against strychnine and picrotoxin. The significance of the glycerol group in (I) and (II) in muscle-relaxing and anticonvulsant actions was discussed. SHOZABURO KITAOKA (Chem. Abstr.)

Action of the Adrenocorticotropic Hormone (ACTH) on the Electrical Activity of the Brain. Monnier, Marcel. [*Rev. méd. Suisse romande*, **73**, 511 (1953).]

ACTH causes modifications of the electrical activity of the rabbit brain which are defined as a function of the injected dose and of its duration of action. Early alterations consist in a thalamocortical activation and late modification consist in depression of electrogenesis which may be a prelude to the death of the animal.

MIREILLE CASTAMBIDE-ODIER (Chem. Abstr.)

Action of Diethylstilbestrol on the Hypothalamic Neurosecretion of the Female White Rat. Stutinsky, F. [*Ann. endocrinol.*, **14**, 101 (1953).]

Injection of large doses of diethylstilbestrol increases the neurocytogenous secretion of the hypothalamus and of the neurohypophysis. This phenomenon is morphologically revealed by Gomor's chromic hematoxylin. The histological modifications parallel the hyperproduction and hypersecretion of the antidiuretic hormone, whereas the oxytocic principle seems to be diminished in the neurohypophysis. Progesterone produces modifications of the histological aspect of the hypothalamus and neurohypophysis which are in every respect contrary to those engendered by injections of distilbene. MIREILLE CASTAMBIDE-ODIER (Chem. Abstr.)

The Action of Narcotic and Convulsive Agents on the Brain of Cold-blooded Animals Previously Treated with Acetylcholine. Muller-Limmroth, Heinz Wolf and Massmann, Helmut. [*Pflugers Arch. ges. Physiol.*, **255**, 379 (1952).]

Frogs were injected intraperitoneally with high doses (0·005 mg./g.) of acetylcholine (I). A further injection 10 minutes later of 1 ml. 25 per cent. ethylurethan (II) or of 0·75 ml. of 0·1 per cent. strychnine (III) was injected into the lymph sac. After another 10 minutes, the frogs were decapitated and electroencephalographic tracings recorded. (I) Increased the frequency and the regularity of the waves. (II) Reduced the activity to a barely detectable level. (III) Increased both the frequency and the amplitude of the waves. The normal duration of bioelectrical activity of the brain from (I)-treated frogs was 26-27 minutes. With (I) plus (II), this was shortened to 3·5 minutes and with (I) plus (III), lengthened to 40 minutes. The normal brain K was 401 mg. per cent. The brain of (I)-treated frogs contained 373 mg. per cent. (I) plus (II) caused a fall to 305 mg. per cent. and (I) plus (III) produced a rise to 454 mg. per cent. HERMAN I. CHINN (Chem. Abstr.)